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FIFTH EDITION

PARK'S THE PEDIATRIC CARDIOLOGY HANDBOOK

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FIFTH EDITION

PARK'S THE PEDIATRIC CARDIOLOGY HANDBOOK

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DEDICATION

To my loving wife, Issun

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Preface to Fifth Edition

Since the publication of the fourth edition of *The Pediatric Cardiology Handbook*, important advances have been made in both the diagnosis and treatment of children with congenital and acquired heart diseases. These advances make it necessary to update the handbook. Although extensive updating and revisions have been made throughout the book, the handbook maintains its original goal of providing readers with fundamental and practical information in the management of children with cardiac problems.

Although every topic and chapter has been updated, certain congenital heart defects received more extensive revision, including infective endocarditis, cardiomyopathies, cardiac arrhythmias, and long QT syndrome. A major revision has been made in dyslipidemias with inclusion of the new recommendations on lipid screening for children. Sections on blood pressure and systemic hypertension have been extensively rewritten. Normative blood pressure standards for auscultometric and oscillometric methods obtained in the San Antonio Children's Blood Pressure Study are recommended because they are the only standards obtained by the currently recommended methods. For the chapter on electrocardiography, normative data used are from the recently revised fourth edition of my book *How to Read Pediatric ECGs*. The two-dimensional echocardiographic section has been expanded and detailed normative values of echocardiography are included in Appendix D. In the area of cardiac surgery, new approaches such as hybrid procedures have been updated and the recommended timing of some procedures has been updated.

I wish to acknowledge the contributions of the following individuals in the revision. Dr. Mehrdad Salamat, MD, Attending Cardiologist at the Driscoll Children's Hospital and Clinical Associate Professor of Pediatrics, Texas A&M University Health Science Center, has updated two chapters in the "Cardiac Surgical Patients" section. Dr. Salamat was also instrumental in updating drug dosages with the addition of newer drugs that are used in the practice of pediatric cardiology. Paula Scott, PhD, MLS, and Cindy Munoz, BA, librarians at the Driscoll Children's Hospital, helped me with literature search throughout the project. Linda Lopez, a cardiac sonographer (and the manager of Driscoll's McAllen Cardiology Clinic) provided me with valuable suggestions on the echocardiographic illustrations. Most of all, I thank my wife, Issun, for her understanding during my long period of preoccupation with the project.

I believe this handbook will be an important companion to cardiology fellows, pediatricians, family practitioners, house staff, and medical students. This handbook will also serve well any health care providers who deal with children, including physician assistants, nurse practitioners, and nursing students. This handbook may prove to be a very useful compendium even for practicing cardiologists because it makes basic and advanced information in the practice of cardiology available instantly.

Myung K. Park, MD, FAAP, FACC

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BASIC TOOLS IN EVALUATION OF CARDIAC PATIENTS

Initial evaluation of children with possible cardiac problems includes (1) history taking, (2) physical examination, (3) electrocardiographic (ECG) evaluation, and (4) chest radiography. Many cardiologists obtain an echocardiogram (echo), instead of a radiograph, for initial complete cardiac evaluation. The weight of information gained from these techniques varies with the type and severity of the disease.

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Chapter 1

History and Physical Examination

I. HISTORY TAKING

A. Gestational and Perinatal History

Prenatal (gestational), perinatal, postnatal, past, and family histories should be obtained.

1. Maternal infection: Rubella during the first trimester of pregnancy commonly results in PDA and PA stenosis (rubella syndrome, see [Table 1-1](#)). Other viral infections early in pregnancy may be teratogenic. Viral infections (including human immunodeficiency virus) in late pregnancy may cause myocarditis.
2. Maternal medications: The following is a partial list of suspected teratogenic drugs that cause CHDs.
 - a. Amphetamines (VSD, PDA, ASD, and TGA), phenytoin (PS, AS, COA, and PDA), trimethadione (fetal trimethadione syndrome: TGA, VSD, TOF, HLHS, see [Table 1-1](#)), lithium (Ebstein's anomaly), retinoic acid (conotruncal anomalies), valproic acid (various noncyanotic defects), and progesterone or estrogen (VSD, TOF, and TGA) are highly suspected teratogens.
 - b. Warfarin may cause fetal warfarin syndrome (TOF, VSD, and other features such as ear abnormalities, cleft lip or palate, and hypoplastic vertebrae) (see [Table 1-1](#)).
 - c. Excessive maternal alcohol intake may cause fetal alcohol syndrome (in which VSD, PDA, ASD, and TOF are common) (see [Table 1-1](#)).
 - d. Cigarette smoking causes intrauterine growth retardation but not CHD.
3. Maternal conditions:
 - a. Maternal diabetes increases the incidence of CHD (TGA, VSD, and PDA) and cardiomyopathy (see [Table 1-1](#)).
 - b. Maternal lupus erythematosus and collagen diseases have been associated with congenital heart block in the offspring.
 - c. History of maternal CHD may increase the prevalence of CHD in the offspring to as much as 15%, compared with 1% in the general population (see Appendix, Table A-2).

B. Postnatal and Present History

1. Poor weight gain and delayed development may be caused by CHF, severe cyanosis, or general dysmorphic conditions. Weight is more affected than height.
2. Cyanosis, squatting, and cyanotic spells suggest TOF or other cyanotic CHD.

TABLE 1-1

MAJOR SYNDROMES ASSOCIATED WITH CARDIOVASCULAR ABNORMALITIES

DISORDERS	CV ABNORMALITIES: FREQUENCY AND TYPES	MAJOR FEATURES	ETIOLOGY
Alagille Syndrome (Arteriohepatic Dysplasia)	Frequent (85%); peripheral PA stenosis with or without complex CV abnormalities	Peculiar facies (95%) consisting of deep-set eyes; broad forehead; long straight nose with flattened tip; prominent chin; small, low-set malformed ears. Paucity of intrahepatic interlobular bile duct with chronic cholestasis (91%), hypercholesterolemia, butterfly-like vertebral arch defects (87%). Growth retardation (50%) and mild mental retardation (16%).	AD Chromosome 22q11.2
CHARGE Association	Common (65%); TOF, truncus arteriosus, aortic arch anomalies (e.g., vascular ring, interrupted aortic arch)	C oloboma, h ear defects, choanal a tresia, growth or mental retardation, g enitourinary anomalies, e ar anomalies, genital hypoplasia	8q12 deletion
Carpenter Syndrome	Frequent (50%); PDA, VSD, PS, TGA	Brachycephaly with variable craniosynostosis, mild facial hypoplasia, polydactyly and severe syndactyly ("mitten hands")	AR
Cockayne Syndrome	Accelerated atherosclerosis	Senile-like changes beginning in infancy, dwarfing, microcephaly, prominent nose and sunken eyes, visual loss (retinal degeneration) and hearing loss	AR
Cornelia de Lange (de Lange) Syndrome	Occasional (30%); VSD	Synophrys and hirsutism, prenatal growth retardation, microcephaly, anteverted nares, downturned mouth, mental retardation	Unknown; AD?
Cri Du Chat Syndrome (Deletion 5p Syndrome)	Occasional (25%); variable CHD (VSD, PDA, ASD)	Catlike cry in infancy, microcephaly, downward slant of palpebral fissures	Partial deletion, short arm of chromosome 5
Crouzon Disease (Craniofacial Dysostosis)	Occasional; PDA, COA	Ptois with shallow orbits, premature craniosynostosis, maxillary hypoplasia	AD
DiGeorge Syndrome (Overlap with Velocardiofacial Syndrome)	Frequent; interrupted aortic arch, truncus arteriosus, VSD, PDA, TOF	Hypertelorism, short philtrum, downslanting eyes, hypoplasia or absence of thymus and parathyroid, hypocalcemia, deficient cell-mediated immunity	Microdeletion of 22q11.2

Down Syndrome (Trisomy 21)	Frequent (40%-50%); ECD, VSD	Hypotonic, flat facies, slanted palpebral fissure, small eyes, mental deficiency, simian crease	Trisomy 21
Ehlers-Danlos Syndrome	Frequent; ASD, aneurysm of aorta and carotids, intracranial aneurysm, MVP	Hyperextensive joints, hyperelasticity, fragility and bruisability of skin, poor wound healing with thin scar	AD
Ellis-van Creveld Syndrome (Chondroectodermal Dysplasia)	Frequent (50%); ASD, single atrium	Short stature of prenatal onset, short distal extremities, narrow thorax with short ribs, polydactyly, nail hypoplasia, neonatal teeth	AR
Fetal Alcohol Syndrome	Occasional (25%-30%); VSD, PDA, ASD, TOF	Prenatal growth retardation, microcephaly, short palpebral fissure, mental deficiency, irritable infant or hyperactive child	Ethanol or its byproducts
Fetal Trimethadione Syndrome	Occasional (15%-30%); TGA, VSD, TOF	Ear malformation, hypoplastic midface, unusual eyebrow configuration, mental deficiency, speech disorder	Exposure to trimethadione
Fetal Warfarin Syndrome	Occasional (15%-45%); TOF, VSD	Facial asymmetry and hypoplasia, hypoplasia or aplasia of the pinna with blind or absent external ear canal (microtia), ear tags, cleft lip or palate, epitubular dermoid, hypoplastic vertebrae	Exposure to warfarin
Friedreich Ataxia	Frequent; hypertrophic cardiomyopathy progressing to heart failure	Late-onset ataxia, skeletal deformities	AR
Goldenhar Syndrome (Oculoauriculovertebral Spectrum)	Frequent (35%); VSD, TOF	Facial asymmetry and hypoplasia, microtia, eartag, cleft lip/palate, hypoplastic vertebrae	Unknown; usually sporadic
Glycogen Storage Disease II (Pompe Disease)	Very common; cardiomyopathy	Large tongue and flabby muscles, cardiomegaly; LVH and short PR on ECG, severe ventricular hypertrophy on echo; normal FBS and GTT	AR
Holt-Oram Syndrome (Cardio-limb Syndrome)	Frequent; ASD, VSD	Defects or absence of thumb or radius	AD
Homocystinuria	Frequent; medial degeneration of aorta and carotids, atrial or venous thrombosis	Subluxation of lens (usually by 10 yr), malar flush, osteoporosis, arachnodactyly, pectus excavatum or carinatum, mental defect	AR
Infant of Diabetic Mother	CHDs (3%-5%); TGA, VSD, COA; cardiomyopathy (10%-20%); PPHN	Macrosomia, hypoglycemia and hypocalcemia, polycythemia, hyperbilirubinemia, other congenital anomalies	Fetal exposure to high glucose levels

Continued

TABLE 1-1

MAJOR SYNDROMES ASSOCIATED WITH CARDIOVASCULAR ABNORMALITIES (Continued)

DISORDERS	CV ABNORMALITIES: FREQUENCY AND TYPES	MAJOR FEATURES	ETIOLOGY
Kartagener Syndrome	Dextrocardia	Situs inversus, chronic sinusitis and otitis media, bronchiectasis, abnormal respiratory cilia, immotile sperm	AR
LEOPARD Syndrome (Multiple Lentigenes Syndrome)	Very common; PS, HOCM, long PR interval	<i>L</i> entiginous skin lesion, <i>E</i> CG abnormalities, <i>a</i> cular hypertelorism, <i>p</i> ulmonary stenosis, <i>a</i> bnormal genitalia, <i>r</i> etarded growth, <i>d</i> eafness	AD
Long QT Syndrome: Jervell and Lange-Nielsen Syndrome	Very common; long QT interval on ECG, ventricular tachyarrhythmia	Congenital deafness (not in Romano-Ward syndrome), syncope resulting from ventricular arrhythmias, family history of sudden death (\pm)	AR AD
Romano-Ward Syndrome			
Marfan's Syndrome	Frequent; aortic aneurysm, aortic and/or mitral regurgitation	Arachnodactyly with hypextensibility, subluxation of lens	AD
Mucopolysaccharidosis	Frequent; aortic and/or mitral regurgitation, coronary artery disease	Coarse features, large tongue, depressed nasal bridge, kyphosis, retarded growth, hepatomegaly, corneal opacity (not in Hunter syndrome), mental retardation; most patients die by 10 to 20 years of age	AR XR AR
Hurler Syndrome (Type I)			
Hunter Syndrome (Type II)			
Morquio Syndrome (Type IV)			
Muscular Dystrophy (Duchenne Type)	Frequent; cardiomyopathy	Waddling gait, "pseudohypertrophy" of calf muscle	XR
Neurofibromatosis (von Recklinghausen Disease)	Occasional; PS, COA, pheochromocytoma	Cafe-au-lait spots, multiple neurofibroma, acoustic neuroma, variety of bone lesions	AD
Noonan Syndrome (Turner-like Syndrome)	Frequent; PS (dystrophic pulmonary valve), LVH (or anterior septal hypertrophy)	Similar to Turner syndrome but may occur both in males and females, without chromosomal abnormality	Usually sporadic; apparent AD?
Pierre Robin Syndrome	Occasional; VSD, PDA; less commonly ASD, COA, TOF	Micrognathia, glossoptosis, cleft soft palate	In utero mechanical constraint?

Osler-Weber-Rendu Syndrome (Hereditary Hemorrhagic Telangiectasia)	Occasional; pulmonary arteriovenous fistula	Hepatic involvement, telangiectases, hemangioma or fibrosis	AD
Osteogenesis Imperfecta	Occasional; aortic dilatation, aortic regurgitation, MVP	Excessive bone fragility with deformities of skeleton, blue sclera, hyperlaxity of joints	AD/AR
Progeria (Hutchinson-Gilford Syndrome)	Accelerated atherosclerosis	Alopecia, atrophy of subcutaneous fat, skeletal hypoplasia and dysplasia	Unknown; occasional AD or AR
Rubella Syndrome	Frequent (>95%); PDA and PA stenosis	Triad of the syndrome: deafness, cataract, and CHDs; others include intrauterine growth retardation, microcephaly, microphthalmia, hepatitis, neonatal thrombocytopenic purpura	Maternal rubella infection during the first trimester
Rubinstein-Taybi Syndrome	Occasional (25%); PDA, VSD, ASD	Broad thumbs or toes; hypoplastic maxilla with narrow palate; beaked nose, short stature, mental retardation	Sporadic; 16p13.3 deletion
Smith-Lemli-Opitz Syndrome	Occasional; VSD, PDA, others	Broad nasal tip with anteverted nostrils, ptosis of eyelids, syndactyly of 2nd and 3rd toes, short stature, mental retardation	AR
Thrombocytopenia-Absent Radius (TAR) Syndrome	Occasional (30%); TOF, ASD, dextrocardia	Thrombocytopenia, absent or hypoplastic radius, normal thumb; "leukemoid" granulocytosis and eosinophilia	AR
Treacher Collins Syndrome	Occasional; VSD, PDA, ASD	Defects of lower lids, malar hypoplasia with downslanting palpebral fissure, malformation of auricle or ear canal defect, cleft palate	Fresh mutation; AD
Trisomy 13 Syndrome (Patau Syndrome)	Very common (80%); VSD, PDA, dextrocardia	Low birth weight, central facial anomalies, polydactyly, chronic hemangiomas, low-set ears, visceral and genital anomalies	Trisomy 13
Trisomy 18 Syndrome (Edward Syndrome)	Very common (90%); VSD, PDA, PS	Low birth weight, microcephaly, micrognathia, rocker-bottom feet, closed fist with overlapping fingers	Trisomy 18
Tuberous Sclerosis	Frequent; thabdomyoma	Triad of adenoma sebaceum (2-5 yr of age), seizures, and mental defect; cystlike lesions in phalanges and elsewhere; fibrous-angiomas lesions (83%) with varying colors in nasolabial fold, cheeks, and elsewhere	AD

Continued

TABLE 1-1

MAJOR SYNDROMES ASSOCIATED WITH CARDIOVASCULAR ABNORMALITIES (Continued)

DISORDERS	CV ABNORMALITIES: FREQUENCY AND TYPES	MAJOR FEATURES	ETIOLOGY
Turner Syndrome (XO Syndrome)	Frequent (35%); COA, bicuspid aortic valve, AS; hypertension, aortic dissection later in life	Short female; broad chest with widely spaced nipples; congenital lymphedema with residual puffiness over the dorsum of fingers and toes (80%).	XO with 45 chromosomes
VATER Association (VATER/VACTERL Syndrome)	Common (>50%); VSD, other defects	Vertebral anomalies, anal atresia, congenital heart defects, tracheoesophageal (TE) fistula, renal dysplasia, limb anomalies (e.g., radial dysplasia)	Sporadic
Velocardiofacial Syndrome (Splintzen Syndrome)	Very common (85%); truncus arteriosus, TOF, pulmonary atresia with VSD, interrupted aortic arch (type B), VSD, and D-TGA	Structural or functional palatal abnormalities, unique facial characteristics ("elfin facies" with auricular abnormalities, prominent nose with squared nasal root and narrow alar base, vertical maxillary excess with long face), hypernasal speech, conductive hearing loss, hypotonia, developmental delay and learning disability	Unknown: chromosome 22q11 (probably the same disease as DiGeorge syndrome)
Williams Syndrome	Frequent; supravalvular AS, PA stenosis	Varying degree of mental retardation, so-called "elfin facies" (with upturned nose, flat nasal bridge, long philtrum, flat malar area, wide mouth, full lips, widely spaced teeth, periorbital fullness), hypercalcemia of infancy?	Sporadic; 7q23 deletion; AD?
Zellweger Syndrome (Cerebro-hepatorenal Syndrome)	Frequent; PDA, VSD or ASD	Hypotonia, high forehead with flat facies, hepatomegaly, albuminemia	AR

AD, autosomal dominant; AR, autosomal recessive; AS, aortic stenosis; ASD, atrial septal defect; CHD, congenital heart disease; COA, coarctation of the aorta; CV, cardiovascular; ECD, endocardial cushion defect; ECG, electrocardiogram; FBS, fasting blood sugar; GTT, glucose tolerance test; HOCM, hypertrophic obstructive cardiomyopathy; LVH, left ventricular hypertrophy; MR, mitral regurgitation; MVP, mitral valve prolapse; PA, pulmonary artery; PDA, patent ductus arteriosus; PFC, persistent fetal circulation; PPHN, persistent pulmonary hypertension of newborn; PS, pulmonary stenosis; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect; XR, sex-linked recessive; ±, may or may not be present.

From Park MK: Park's Pediatric Cardiology for Practitioners, ed 6, Philadelphia, Mosby, 2014.

3. Tachycardia, tachypnea, and puffy eyelids are signs of CHF.
4. Frequent lower respiratory tract infections may be associated with large L-R shunt lesions.
5. Decreased exercise tolerance may be a sign of significant heart defects or ventricular dysfunction.
6. Heart murmur. The time of its first appearance is important. A heart murmur noted shortly after birth indicates a stenotic lesion (AS, PS). A heart murmur associated with large L-R shunt lesions (such as VSD or PDA) may be delayed. Appearance of a heart murmur in association with fever suggests an innocent heart murmur.
7. Chest pain. Ask if chest pain is exercise-related or nonexertional. Also ask about its duration, nature, and radiation. Nonexertional chest pain is unlikely to have cardiac causes (except for pericarditis). Cardiac causes of chest pain are usually exertional and are very rare in children and adolescents. The three most common causes of noncardiac causes of chest pain in children are costochondritis, trauma to chest wall or muscle strain, and respiratory diseases (see Chest Pain in Chapter 20).
8. Palpitation may be caused by paroxysms of tachycardia, sinus tachycardia, single premature beats; rarely hyperthyroidism or MVP (see Chapter 22).
9. Joint pain. Joints that are involved, presence of redness and swelling, history of trauma, duration of the pain, and migratory or stationary nature of the pain are important. History of recent sore throat and rashes and family history of rheumatic fever are frequent in acute rheumatic fever. History of rheumatoid arthritis is also an important clue to the diagnosis.
10. Neurologic symptoms. Stroke may result from embolization of thrombus from infective endocarditis, polycythemia, or uncorrected or partially corrected cyanotic CHD. Headache may be associated with polycythemia or rarely with hypertension. Choreic movement may result from rheumatic fever. Fainting or syncope may be due to vasovagal responses, arrhythmias, long QT syndrome, epilepsy, or other noncardiac conditions (see Syncope in Chapter 21).
11. Medications, cardiac and noncardiac (name, dosage, timing, and duration).
12. Syndromes and diseases of other systems with associated cardiovascular abnormalities are summarized in [Tables 1-1 and 1-2](#), respectively.

C. Family History

1. Certain hereditary diseases may be associated with varying frequency of cardiac anomalies ([Table 1-1](#)).
2. CHD in the family. The following provides some information on the chance of occurrence of CHD in the family when family history is positive for CHD.
 - a. The incidence of CHD in the general population is about 1% (8 to 12 per 1000 live births). When one child is affected, the risk of recurrence in siblings is increased to about 3% (see [Table A-1](#) in Appendix).

TABLE 1-2**INCIDENCE OF ASSOCIATED CHDs IN PATIENTS WITH OTHER SYSTEMS' MALFORMATIONS**

ORGAN SYSTEM AND MALFORMATION	FREQUENCY (%)	SPECIFIC CARDIAC DEFECT
CENTRAL NERVOUS SYSTEM		
Hydrocephalus	6	VSD, ECD, TOF
Dandy-Walker syndrome	3	VSD
Agenesis of corpus callosum	15	No specific defect
Meckel-Gruber syndrome	14	No specific defect
THORACIC CAVITY		
TE fistula, esophageal atresia	21	VSD, ASD, TOF
Diaphragmatic hernia	11	No specific defect
GASTROINTESTINAL SYSTEM		
Duodenal atresia	17	No specific defect
Jejunal atresia	5	No specific defect
Anorectal anomalies	22	No specific defect
Imperforate anus	12	TOF, VSD
VENTRAL WALL		
Omphalocele	21	No specific defect
Gastroschisis	3	No specific defect
GENITOURINARY SYSTEM		
Renal agenesis		
Bilateral	43	No specific defect
Unilateral	17	No specific defect
Horseshoe kidney	39	No specific defect
Renal dysplasia	5	No specific defect

ECD, endocardial cushion defect; TE, tracheoesophageal. Other abbreviations are listed in pp. xi-xii. Adapted from Copel JA, Kleinman CS: Congenital heart disease and extracardiac anomalies: Association and indications for fetal echocardiography. *Am J Obstet Gynecol* 154:1121-1132, 1986.

- b. However, the risk of recurrence is related to the incidence of particular defects: lesions with high prevalence (e.g., VSD) tend to have a high risk of recurrence, and those with low prevalence (e.g., tricuspid atresia, persistent truncus arteriosus) have a low risk of recurrence (see Appendix, Table A-1).
- c. The probability of recurrence is substantially higher when the mother, rather than the father, is the affected parent (see Appendix, Table A-2). Tables A-1 and A-2 can be used for counseling.

II. PHYSICAL EXAMINATION**A. Inspection**

1. General appearance. Happy or cranky, nutritional state, respiratory status such as tachypnea, dyspnea, or retraction (they may be signs of serious CHD), pallor (seen with vasoconstriction from CHF or circulatory shock, or severe anemia), and sweat on the forehead (seen in CHF).
2. Inspection for any known syndromes or conditions (see [Table 1-1](#)).

3. Malformations of other systems may be associated with varying frequency of CHD (see [Table 1-2](#)).
4. Acanthosis nigricans (a dark pigmentation of skin crease on the neck) is often seen in obese children and those with type 2 diabetes and may signify the presence of hyperinsulinemia.
5. Precordial bulge, with or without actively visible cardiac activity, suggests chronic cardiac enlargement. Pectus excavatum may be a cause of a heart murmur. Pectus carinatum is usually not a result of cardiomegaly.
6. Cyanosis usually signals a serious CHD. A long-standing arterial desaturation (usually more than 6 months), even of a subclinical degree, results in clubbing of the fingers and toes.

B. Palpation

1. Precordium
 - a. A hyperactive precordium is characteristic of heart diseases with high volume overload, such as L-R shunt lesions or severe valvular regurgitation.
 - b. A thrill is often of real diagnostic value. The location of the thrill suggests certain cardiac anomalies: upper left sternal border (ULSB), PS; upper right sternal border (URSB), AS; lower left sternal border (LLSB), VSD; suprasternal notch, AS, occasionally PS, PDA, or COA; over the carotid arteries, AS or COA.
2. Peripheral pulses
 - a. Check the peripheral pulse for the rate, irregularities (arrhythmias), and volume (bounding, full, or thready).
 - b. Strong arm pulses and weak leg pulses suggest COA.
 - c. The right brachial artery pulse stronger than the left brachial artery pulse may suggest COA or supraaortic AS.
 - d. Bounding pulses are found in aortic runoff lesions (e.g., PDA, AR, large systemic AV fistula).
 - e. Weak and thready pulses are found in CHF and circulatory shock.

C. Blood Pressure

Every child should have blood pressure (BP) measurement as part of the physical examination whenever possible. To determine if the obtained BP level is normal or abnormal, BP readings are compared with reliable BP standards. Unfortunately, there have been problems and confusion regarding the correct method of measuring BP and the reliable normative BP values for children. Arm length–based BP cuff selection methods recommended by two earlier NIH Task Forces (1977 and 1987) are scientifically unsound, and they have contributed to the lack of reliable normative BP standards for decades. Although the Working Group of the National High Blood Pressure Education Program (NHBPEP) has recently corrected the BP cuff selection method, their normative BP data are scientifically and logically unsound (see the following).

1. The following are currently recommended BP measurement techniques.
 - a. The width of the BP cuff should be 40% to 50% of the circumference of the arm (or leg) with the cuff long enough to completely or nearly completely encircle the extremity.
 - b. The NHBPEP recommends Korotkoff phase 5 (K5) as the diastolic pressure but this is debatable. Earlier studies indicate that K4 agrees better with true diastolic pressure for children ≤ 12 years.
 - c. Averaging of 2 or more readings should be obtained.
 - d. The child should be in sitting position with the arm at the heart level.
2. BP Standards Recommended by the NHBPEP.

The normative BP standards recommended by the Working Group are not as good as was suggested. The readers should be aware of a few major flaws in the NHBPEP's normative values.

- a. First of all, BP data presented in the NHBPEP standards are not obtained by using the same methodology as the Program has recommended. They are obtained using the arm length-based cuff selection method, which has been abandoned because of its unscientific nature. These values are also from single measurement, rather than the averages of multiple readings, as currently recommended. They also are not from a nationally representative population.
- b. Expressing children's BP levels by age and height percentiles is statistically and logically unsound. Height has no statistically important role in children's BP levels.
 - (1) Partial correlation analysis done in the San Antonio Children's Blood Pressure Study (SACBPS) shows that, when auscultatory BP levels were adjusted for age and weight, the correlation coefficient of systolic BP with height was very small ($r = 0.068$ for boys; $r = 0.072$ for girls), whereas when adjusted for age and height, the correlation of systolic pressure with weight remained high ($r = 0.343$ for boys; $r = 0.294$ for girls). These findings indicate that the contribution of height to BP levels is negligible. The apparent correlation of height to BP levels may be secondary to a close correlation that exists between height and weight ($r = 0.86$).
 - (2) A similar conclusion was reached with oscillometric BP levels in the same study. Thus, we have recommend children's BP value be expressed as a function of age only, as has been done earlier by NIH Task Forces.
- c. Recommending additional computations and using scientifically unsound complex BP tables on such highly variable office BP readings is unreasonable and counterproductive. Analyzing unscientifically obtained data by additional computation does not improve the worth of the data.
- d. The NHBPEP does not point out that the auscultatory and oscillometric BP readings are not interchangeable. SACBPS, in which both auscultatory and oscillometric methods were used, found that oscillometric systolic pressures are significantly higher than auscultatory BP readings (see below for further details).

- e. The NHBPEP does not emphasize the important contribution of “white coat phenomenon” in office BP readings. White-coat phenomenon is probably the most common cause of high blood pressure readings in pediatric practice.
3. Reliable normative BP standards. Which normal BP standards should be used and why?
- a. The NIH Task Force BP standards (of 1987) are no longer acceptable because they were obtained by using the arm length–based BP cuff selection method.
 - b. The BP standards of the NHBPEP are riddled with major flaws as outlined in the preceding section. These standards reflect violation of basic scientific principles. Although not acceptable as reliable pediatric BP standards, the NHBPEP’s normative values are presented in Appendix B for the sake of completeness (Tables B-1 and B-2, Appendix B).
 - c. Normative BP percentile values from the San Antonio Study (SACBPS) are recommended as better BP standards than the NHBPEP’s standards until nationwide data using the currently recommended methods become available. These are the only available BP standards that have been obtained according to the currently recommended method. In the SACBPS, BP levels were obtained in over 7000 tri-ethnic school children enrolled in kindergarten through the 12th grade in the San Antonio, Texas, area. Both the auscultatory and oscillometric (model Dinamap 8100) methods were used in the study. The data are the averages of three readings. Auscultatory BP data were expressed according to age and gender. These BP standards are normally distributed from the mean value and thus the effect of obesity is not a problem in using the standards (Figs. 1-1 and 1-2). Percentile BP values for these figures are presented in Appendix B (Tables B-3 and B-4).
 - d. When BP is measured using an oscillometric device, one should use a device-specific normative BP standards. SACBPS found that the readings by auscultatory method and by Dinamap 8100 are significantly different and thus are not interchangeable. Percentile BP values by an oscillometric method (Dinamap 8100) are presented in Appendix B (Tables B-5 and B-6).
4. Accuracy of oscillometric BP values.
- a. The accuracy of indirect BP measurement by an oscillometric method (Dinamap Model 1846) has been demonstrated. One caution is that not all oscillometric devices in clinical use have been validated for their accuracy. Accuracy of oscillometric BP does not mean that BPs obtained by the oscillometric method should agree with those obtained by the auscultatory method. Auscultatory BP method is another indirect BP measurement method using a different detection device; only direct intraarterial BP measurement is the gold standard.
 - b. SACBPS found that BP levels obtained by the Dinamap (Model 8100) were on the average 10 mm Hg higher than the auscultatory

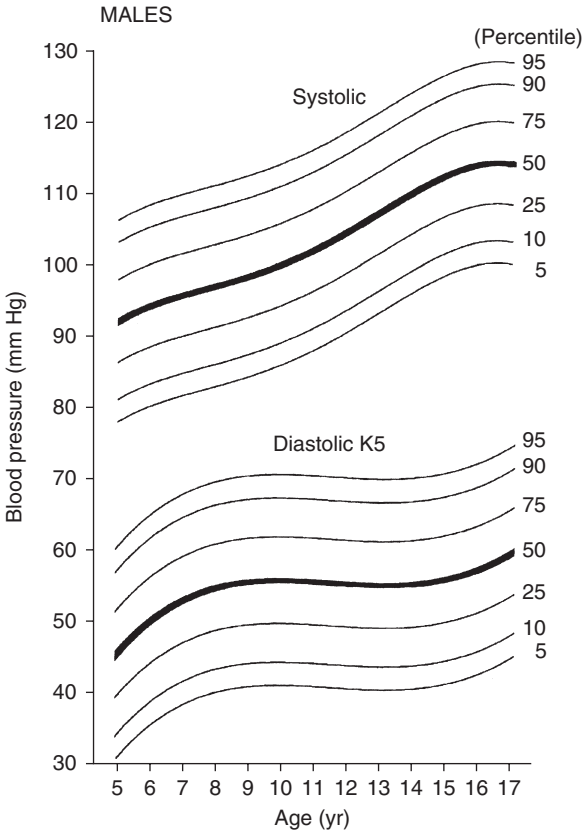
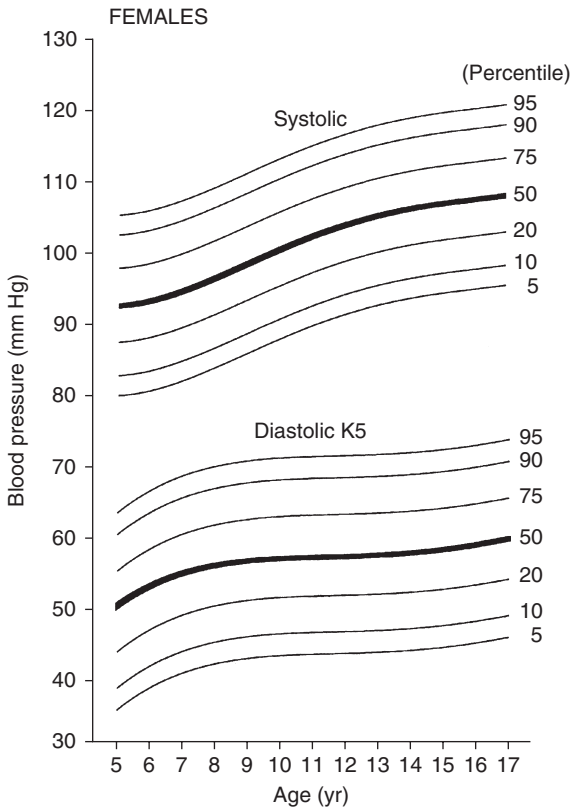


FIGURE 1-1

Age-specific percentile curves of auscultatory systolic and diastolic (K5) pressures in boys 5 to 17 years of age. BP values are the averages of three readings. The width of the BP cuff was 40% to 50% of the circumference of the arm. (From Park MK, Menard SW, Yuan C: Comparison of blood pressure in children from three ethnic groups. *Am J Cardiol* 2001;87:1305-1308.)

method for the systolic pressure and 5 mm Hg higher for the diastolic pressure. Therefore, the auscultatory and the Dinamap BPs are not interchangeable. This does not mean, however, that the oscillometric BP methods are less reliable than the auscultatory method.

- c. Therefore, oscillometric specific normative BP standards are needed. One should not use normative auscultatory BP standards when an

**FIGURE 1-2**

Age-specific percentile curves of auscultatory systolic and diastolic (K5) pressures in girls 5 to 17 years of age. BP values are the averages of three readings. The width of the BP cuff was 40% to 50% of the circumference of the arm. (From Park MK, Menard SW, Yuan C: *Comparison of blood pressure in children from three ethnic groups*. *Am J Cardiol* 2001;87:1305-1308.)

oscillometric method is used. Dinamap 8100 specific BP standards are presented in Appendix B (see Tables B-5 and B-6).

- d. The oscillometric method also provides some advantages over the auscultation method.

- (1) It eliminates observer-related variations.

- (2) It can be successfully used in infants and small children. Auscultatory BP measurement in small infants is not only difficult to obtain but also not accurate.

TABLE 1-3

NORMATIVE BLOOD PRESSURE LEVELS [SYSTOLIC/DIASTOLIC (MEAN)] (mm Hg) BY DINAMAP MONITOR (MODEL 1846 SX) IN CHILDREN UP TO AGE 5 YEARS

AGE	MEAN BP LEVELS	90TH PERCENTILE	95TH PERCENTILE
1-3 days	64/41 (50)	75/49 (59)	78/52 (62)
1 mo-2 yr	95/58 (72)	106/68 (83)	110/71 (86)
2-5 yr	101/57 (74)	112/66 (82)	115/68 (85)

Adapted from Park MK, Menard SM: Normative oscillometric blood pressure values in the first five years in an office setting. *Am J Dis Child* 143:860-864, 1989.

(3) Percentile values of normative oscillometric BPs in neonates and children up to 5 years of age are presented in Appendix B (Table B-7).

5. Comparison of arm and leg BP values.

Four-extremity BP measurements are often obtained in neonates and children to rule out COA.

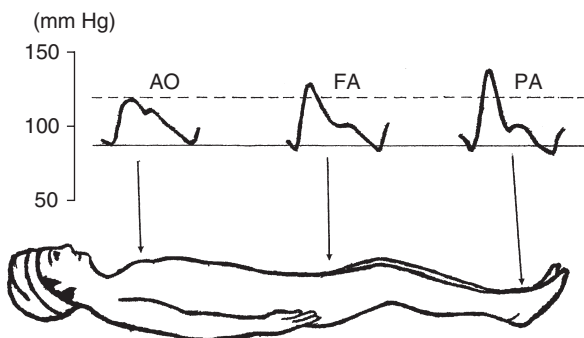
- a. Even with a considerably wider cuff used for the thigh, the Dinamap systolic pressure in the thigh or calf is about 5 to 10 mm Hg higher than that in the arm. This reflects in part the phenomenon of peripheral amplification of systolic pressure (see below). If the systolic pressure is lower in the leg, COA may be present.
- b. In the newborn, the systolic pressures in the arm and the calf are the same. Absence of a higher systolic pressure in the leg in the newborn may be related to the presence of normally narrow aortic isthmus.

6. BP levels in neonates and small children.

- a. BP measurement is important in newborns and small children to diagnose COA, hypertension, or hypotension. In contrast to the recommendations of the NHBEP, the auscultatory method is difficult to apply in newborns and small children because of weak Korotkoff sounds in these age groups, and thus normative auscultatory BP standards are not reliable. Therefore, the oscillometric method is frequently used instead. The same BP cuff selection method as used in older children applies to this age group; i.e., the cuff width approximately 50% of the circumference of the extremity.
- b. Abbreviated normative Dinamap BP standards for newborns and small children (≤ 5 years) are presented in [Table 1-3](#). Full percentile values are presented in Appendix B (Table B-7).

7. The important concept of peripheral amplification of systolic pressure.

Many physicians incorrectly think that peripherally measured BP, such as those measured in the arm, are the same as the central aortic pressure (or the left ventricular pressure). The peripheral systolic pressure, obtained by either direct or indirect method, is not always the same as the central aortic pressure. In fact, arm systolic pressures are in general higher than central aortic pressures, and are much higher in certain situations. This phenomenon is called peripheral amplification of systolic pressure (see [Fig. 1-3](#)). The systolic amplification increases as

**FIGURE 1-3**

Schematic drawing of pulse wave changes seen at different levels of the systemic arteries. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

the site of BP measurement moves distally. The following summarizes key points of the phenomenon.

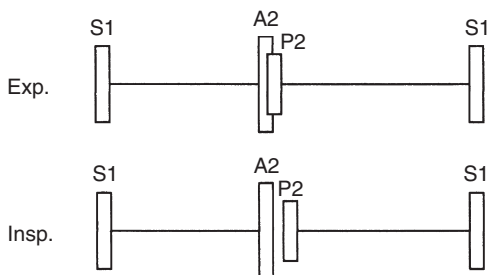
- a. The amplification is limited to the systolic pressure (not in the diastolic and mean pressures).
- b. The systolic amplification is greater in children (with more reactive arteries) than in older adults who may have degenerative arterial disease.
- c. Pedal artery systolic pressures are higher than the radial artery pressures.
- d. The amplification is more marked in vasoconstricted states.
 - (1) Patients in impending circulatory shock (with a high level of circulating catecholamines) may show normal peripheral artery systolic pressure when the central aortic pressure is abnormally low. Early diagnosis of an impending circulatory shock can be missed if one pays attention only to the systolic pressure; monitoring the mean arterial and diastolic pressures should be more useful in this situation.
 - (2) Subjects receiving catecholamine infusion or other vasoconstrictors may show much higher peripheral systolic pressure than the central aortic pressure.
 - (3) A child in congestive heart failure (in which peripheral vasoconstriction exists) may exhibit an exaggerated systolic amplification.
 - (4) Arm systolic pressure in subjects running on treadmills can be markedly higher than the central aortic pressure (see Fig. 5-1).
- e. Reduced level of peripheral amplification of systolic pressure is noted in vasodilated states.
 - (1) Subjects receiving vasodilators.
 - (2) After receiving a contrast dye injection (which has vasodilating effects) during cardiac catheterization.

D. Auscultation

Systematic attention should be given to heart rate and regularity; intensity and quality of the heart sounds, especially the second heart sound; systolic and diastolic sounds (ejection click, midsystolic click, opening snap); and heart murmurs.

1. Heart sounds

- a. The first heart sound (S1) is associated with closure of the mitral and tricuspid valves and is best heard at the apex or LLSB. Splitting of the S1 is uncommon in normal children. Wide splitting of the S1 may be found in RBBB or Ebstein anomaly.
- b. The second heart sound (S2), which is produced by the closure of the aortic and pulmonary valves, is evaluated in the ULSB (or the pulmonary area) in terms of the degree of splitting and the relative intensity of the P2 (the pulmonary closure sound) in relation to the intensity of the A2 (the aortic closure sound). Although best heard with a diaphragm, both components are readily audible with the bell as well.
 - (1) The degree of splitting of the S2 normally varies with respiration, increasing with inspiration and decreasing or becoming single with expiration (Fig. 1-4).
 - (2) Abnormal S2 may take the form of wide splitting, narrow splitting, single S2, abnormal intensity of the P2, or rarely, paradoxical splitting of the S2 (see Box 1-1 for summary of abnormal S2).
- c. The third heart sound (S3) is best heard at the apex or LLSB (Fig. 1-5). It is commonly heard in normal children, young adults, and patients with dilated ventricles and decreased compliance of the ventricles (e.g., large shunt VSD, CHF).
- d. The fourth heart sound (S4) at the apex, which is always pathologic (Fig. 1-5), is audible in conditions with decreased ventricular compliance or CHF.

**FIGURE 1-4**

Relative intensity of the A2 and P2 and the respiratory variation in the degree of splitting of the S2 at the ULSB (pulmonary area). (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

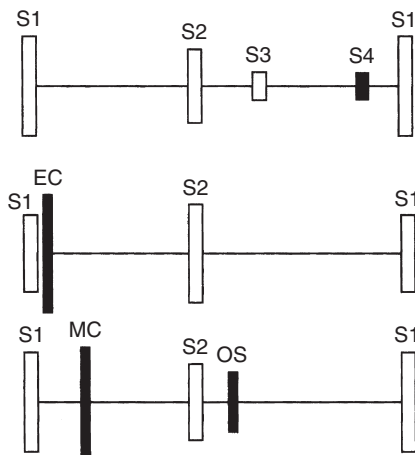
- e. Gallop rhythm generally implies pathology and results from the combination of a loud S3 or S4 and tachycardia. It is common in CHF.
- 2. Systolic and diastolic sounds
 - a. An ejection click sounds like splitting of the S1 but is best audible at the base rather than at the LLSB (Fig. 1-5). The ejection click is associated with stenosis of the semilunar valves (e.g., PS at 2 to 3 LICS, AS at 2 RICS or apex) and enlarged great arteries (e.g., systemic hypertension, pulmonary hypertension, and TOF).
 - b. A midsystolic click with or without a late systolic murmur is heard near the apex in patients with MVP (Fig. 1-5).
 - c. Diastolic opening snap is audible at the apex or LLSB in mitral stenosis (MS) (Fig. 1-5).
- 3. Heart murmurs. Each heart murmur should be analyzed in terms of intensity, timing (systolic or diastolic), location, transmission, and quality (e.g., musical, vibratory, blowing).
 - a. Intensity of the murmur is customarily graded from 1 to 6.
 - (1) Grade 1, barely audible.
 - (2) Grade 2, soft but easily audible.
 - (3) Grade 3, moderately loud but not accompanied by a thrill.

BOX 1-1**SUMMARY OF ABNORMAL S2****ABNORMAL SPLITTING**

- 1. Widely split and fixed S2
 - a. Volume overload (ASD, PAPVR)
 - b. Pressure overload (PS)
 - c. Electrical delay (RBBB)
 - d. Early aortic closure (MR)
 - e. Occasional normal child
- 2. Narrowly split S2
 - a. Pulmonary hypertension
 - b. AS
 - c. Occasional normal child
- 3. Single S2
 - a. Pulmonary hypertension
 - b. One semilunar valve (pulmonary atresia, aortic atresia, persistent truncus arteriosus)
 - c. P2 not audible (TGA, TOF, severe PS)
 - d. Severe AS
 - e. Occasional normal child
- 4. Paradoxically split S2
 - a. Severe AS
 - b. LBBB

ABNORMAL INTENSITY OF P2

- 1. Increased P2 (pulmonary hypertension)
- 2. Decreased P2 (severe PS, TOF, tricuspid stenosis)

**FIGURE 1-5**

Relative position of the heart sounds, ejection click (*EC*), midsystolic click (*MC*), and diastolic opening snap (*OS*). Filled bars show abnormal sounds. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

(4) Grade 4, louder and associated with a thrill.

(5) Grade 5, audible with the stethoscope barely on the chest.

(6) Grade 6, audible with the stethoscope off the chest.

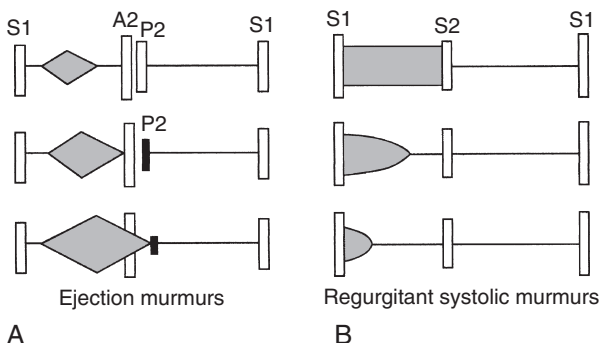
- b. Classification of heart murmurs. Heart murmurs are classified as systolic, diastolic, or continuous.

4. Systolic murmurs

- a. Classification of systolic murmurs. A systolic murmur occurs between S1 and S2. Systolic murmur was initially classified by Aubrey Leatham in 1958 into two types, ejection or regurgitant, depending on the timing of the onset, not the termination, of the murmur in relation to the S1. Recently Joseph Perloff proposed a new classification according to the time of *onset* and *termination* into 4 types: midsystolic (ejection), holosystolic, early systolic, and late systolic.

(1) Ejection systolic murmur (also called stenotic, diamond-shaped or Perloff's midsystolic) has an interval between S1 and the onset of the murmur and is crescendo-decrescendo. The murmur may be short or long (Fig. 1-6, A). These murmurs are caused by flow of blood through stenotic or deformed semilunar valves or increased flow through normal semilunar valves and are therefore found at the base or over the midprecordium. These murmurs may be pathologic or innocent.

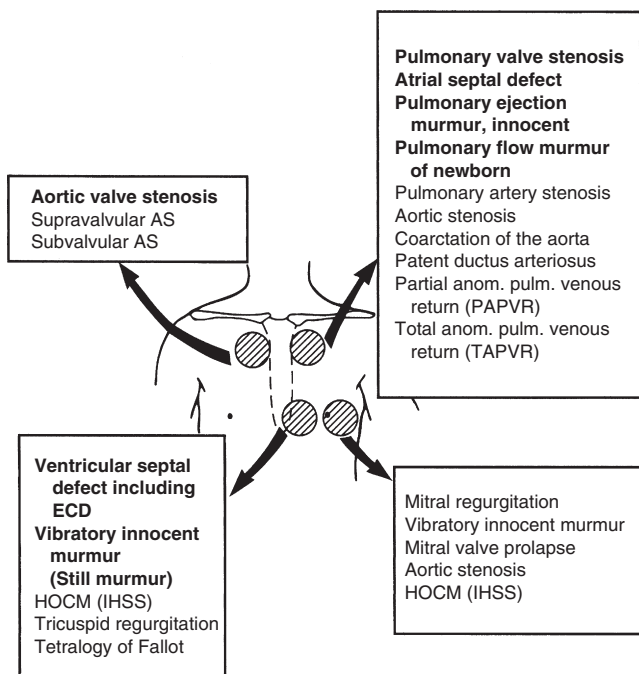
(2) Regurgitant systolic murmur begins with the S1 (no gap between the S1 and the onset of the murmur) and usually lasts throughout

**FIGURE 1-6**

Ejection and regurgitant systolic murmurs. **A**, An ejection systolic murmur is audible in pulmonary valve stenosis (and other conditions). With mild stenosis the apex of the diamond is in the early part of systole (*top*). With increasing severity of obstruction to flow, the murmur becomes louder and longer and its apex moves toward S2 (*middle*). In severe PS, the murmur may last beyond A2 and the P2 is sometimes too soft to be audible (*bottom*). **B**, Regurgitant systolic murmur starts with S1. Most regurgitant systolic murmur in children is due to VSD and is holosystolic, extending all the way to S2 (*top*). In some children, especially those with small VSDs, and some neonates with VSD, the regurgitant systolic murmur may be decrescendo and ends in middle or early systole (not holosystolic) (*middle bottom*), but never crescendo-decrescendo.

systole (pansystolic or holosystolic) but may be decrescendo ending in middle or early systole (Fig. 1-6, B). Perloff's holosystolic and early systolic murmurs are regurgitant murmurs. These murmurs are always pathologic and are associated with only three conditions: VSD, MR, and TR.

- (3) Late systolic murmur of Perloff is the hallmark of MVP (see Fig. 13-4).
- b. Location. In addition to the type of murmur (ejection vs. regurgitant) the location of maximal intensity of the murmur is of great importance in determining the origin of the murmur. Figure 1-7 illustrates systolic murmurs that are audible maximally at the various locations. Tables 1-4 through 1-7 summarize other clinical findings (e.g., physical examination, chest radiography, and ECG) that may aid diagnosis according to the location of a systolic murmur.
- c. Transmission. A systolic ejection murmur at the base that transmits well to the neck is likely to be aortic, and one that transmits well to the sides of the chest and the back is likely to arise in the pulmonary valve or pulmonary artery.
- d. Quality. Ejection systolic murmurs of AS or PS have a rough, grating quality. A common innocent murmur in children (Still murmur) has a characteristic vibratory or humming quality.

**FIGURE 1-7**

Systolic murmurs audible at various locations. More common conditions are shown in **boldface** type (see also [Tables 1-4 through 1-7](#)). (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

5. Diastolic murmurs. Diastolic murmurs occur between S2 and S1. There are the following three types.
 - a. Early diastolic (protodiastolic) decrescendo murmurs are caused by AR or PR ([Fig. 1-8](#)). AR murmurs are high pitched, are best heard at the 3LICS, and radiate to the apex. PR murmurs are usually medium pitched but may be high pitched if pulmonary hypertension is present, best heard at the 2LICS, and they radiate along the left sternal border.
 - b. Middiastolic murmurs are low pitched, starting with a loud S3 ([Fig. 1-8](#)). Best heard with the bell of the stethoscope, these murmurs are caused by anatomic or relative stenosis of the mitral or tricuspid valve. MS murmurs are best heard at the apex (apical rumble), and TS murmurs are heard along the LLSB.
 - c. Presystolic, or late diastolic, murmurs are low pitched and occur late in diastole or just before the onset of systole ([Fig. 1-8](#)). They are found with anatomic stenosis of the mitral or tricuspid valve.

TABLE 1-4

DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS AT THE ULSB (PULMONARY AREA)

CONDITION	IMPORTANT PHYSICAL FINDINGS	CHEST RADIOGRAPHY	ECG FINDINGS
PS	SEM grade 2-5/6 *Thrill (\pm) S2 may split widely when mild *Ejection click (\pm) at 2LICS Transmits to back	*Prominent MPA segment (poststenotic dilation) Normal PVM	Normal if mild, RAD *RVH RAH if severe
ASD	SEM grade 2-3/6 *Widely split and fixed S2	*Increased PVM *RAE and RVE	RAD RVH *RBBB (rsR' in V1)
Pulmonary Flow Murmur of Newborn	SEM grade 1-2/6 No thrill *Good transmission to back and axillae	Normal	Normal
Pulmonary Flow Murmur of Older Children	SEM grade 2-3/6 No thrill Poor transmission	Normal Occasional pectus excavatum or straight back	Normal
Pulmonary Artery Stenosis	SEM grade 2-3/6 Occasional continuous murmur in the back, if severe P2 may be loud *Transmits well to back and both axillae	Prominent hilar vessels (\pm)	RVH or normal
AS	SEM grade 2-5/6 *Also audible in 2RICS *Thrill (\pm) at 2RICS and SSN *Ejection click at apex, 3LICS, or 2RICS (\pm) Paradoxically split S2 if severe	Dilated aorta	Normal or LVH
TOF	*Long SEM, grade 2-4/6 Louder at MLSB *RVH or BVH Loud, single S2 Cyanosis, clubbing (\pm)	*Decreased PVM *Normal heart size Boot-shaped heart Right aortic arch (25%)	RAD *RVH or BVH RAH (\pm)
COA	SEM grade 1-3/6 Loudest at left interscapular area (back) *Weak or absent femorals Hypertension in arms Frequently associated with bicuspid aortic valve, or MR	*Classic 3 sign on plain film or E sign on barium esophagogram Rib notching (\pm)	LVH in children RBBB or RVH in newborns
PDA	*Continuous murmur, grade 2-4/6, at left infraclavicular area Occasional crescendo systolic only Thrill (\pm) Bounding pulses	*Increased PVM *LAE and LVE	Normal, LVH, or BVH

Continued

TABLE 1-4

**DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS AT THE ULSB
(PULMONARY AREA)** (Continued)

CONDITION	IMPORTANT PHYSICAL FINDINGS	CHEST RADIOGRAPHY	ECG FINDINGS
TAPVR	SEM grade 2-3/6 Widely split and fixed S2 (±) *Quadruple or quintuple rhythm Diastolic rumble at LLSB *Mild cyanosis and clubbing (±)	*Increased PVM RAE and RVE Prominent MPA Snowman sign	RAD RAH *RVH
PAPVR	Physical findings similar to those of ASD *S2 may not be fixed unless associated with ASD	Increased PVM *RAE and RVE Scimitar sign (±)	Same as in ASD

*Finding is particularly characteristic of the condition.

BVH, biventricular hypertrophy; 2LICS, second left intercostal space; LVE, left ventricular enlargement; SSN, suprasternal notch; (±), may be present. Other abbreviations are listed on pp. xi-xii.

TABLE 1-5

DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS AT THE URSB (AORTIC AREA)

CONDITION	IMPORTANT PHYSICAL FINDINGS	CHEST RADIOGRAPHY	ECG FINDINGS
Aortic Valve Stenosis	SEM grade 2-5/6 at 2RICS; may be loudest at 3LICS *Thrill (±), URSB, SSN, and carotid arteries *Ejection click *Transmits well to neck S2 may be single	Mild LVE (±) Prominent ascending aorta or aortic knob	Normal or LVH with or without strain
Subaortic Stenosis	SEM grade 2-4/6 *AR murmur may be present No ejection click	Usually normal	Normal or LVH
Supravalvular Aortic Stenosis	SEM grade 2-3/6 Thrill (±) No ejection click *Pulse and BP may be greater in right than left arm *Peculiar facies, mental retardation (±) (in Williams syndrome)	Unremarkable	Normal, LVH, or BVH

*Finding is particularly characteristic of the condition.

BVH, biventricular hypertrophy; 3LICS, third left intercostal space; 2RICS, second right intercostal space; SSN, suprasternal notch; (±), may be present. Other abbreviations are listed on pp. xi-xii.

TABLE 1-6

DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS AT THE LLSB

CONDITION	IMPORTANT PHYSICAL FINDINGS	CHEST RADIOGRAPHY	ECG FINDINGS
VSD	*Regurgitant systolic, grade 2-5/6 May not be holosystolic Well localized at LLSB *Thrill often present P2 may be loud	*Increased PVM *LAE and LVE (cardiomegaly)	Normal LVH or BVH
Complete ECD	Similar to findings of VSD *Diastolic rumble at LLSB *Gallop rhythm common in infants (CHF)	Similar to large VSD	*Superior QRS axis, LVH or BVH
Vibratory Innocent Murmur (Still Syndrome)	SEM grade 2-3/6 *Musical or vibratory with midsystolic accentuation *Maximum between LLSB and apex	Normal	Normal
HOCM or IHSS	SEM grade 2-4/6, medium pitch Maximum LLSB or apex Thrill (±) *Sharp upstroke of brachial pulses May have MR murmur	Normal or globular LVE	LVH Abnormally deep Q waves in V5 and V6
Tricuspid Regurgitation (TR)	*Regurgitant systolic, grade 2-3/6 *Triple or quadruple rhythm (in Ebstein anomaly) Mild cyanosis (±) Hepatomegaly with pulsatile liver and neck vein distention when severe	Normal PVM RAE, if severe	RBBB, RAH, and first-degree AV block in Ebstein anomaly
Tetralogy of Fallot (TOF)	Murmurs can be louder at ULSB (See Table 1-4)	See Table 1-4	See Table 1-4

*Finding is characteristic of the condition.

BVH, biventricular hypertrophy; ECD, endocardial cushion defect; HOCM, hypertrophic obstructive cardiomyopathy; IHSS, idiopathic hypertrophic subaortic stenosis; LVE, left ventricular enlargement; (±), may be present. Other abbreviations are listed on pp. xi-xii.

6. Continuous murmurs. Continuous murmurs begin in systole and continue without interruption through the S2 into all or part of diastole (Fig. 1-8). A combined systolic and diastolic murmur, such as from AS and AR or PS and PR, is called a to-and-fro murmur to distinguish it from a machinery-like continuous murmur. Continuous murmurs are caused by the following:
 - a. Aortopulmonary or arteriovenous connection (e.g., PDA, arteriovenous [AV] fistula, after B-T shunt surgery, or, rarely, persistent truncus arteriosus).
 - b. Disturbances of flow patterns in veins (venous hum).
 - c. Disturbances of flow patterns in arteries (COA, peripheral PA stenosis).

TABLE 1-7
DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS AT THE APEX

CONDITION	IMPORTANT PHYSICAL FINDINGS	CHEST RADIOGRAPHY	ECG FINDINGS
MR	*Regurgitant systolic murmur at apex, grade 2-3/6 Transmits to left axilla (less obvious in children) May be loudest in the midprecordium	LAE and LVE	LAH or LVH
MVP	*Midsystolic click with or without late systolic murmur *High incidence (85%) of thoracic skeletal anomalies (e.g., pectus excavatum, straight back)	Normal	Inverted T in aVF (±)
AS	Murmur and ejection click may be best heard at apex, rather than at 2RICS	(See Table 1-5)	
HOCM or IHSS	Murmur of IHSS may be maximal at apex (may represent MR) (See Table 1-6)		
Vibratory Innocent Murmur	This innocent murmur may be loudest at apex (See Table 1-6)		

*Finding is characteristic of the condition.
(±), may be present. Other abbreviations are listed on pp. xi-xii.

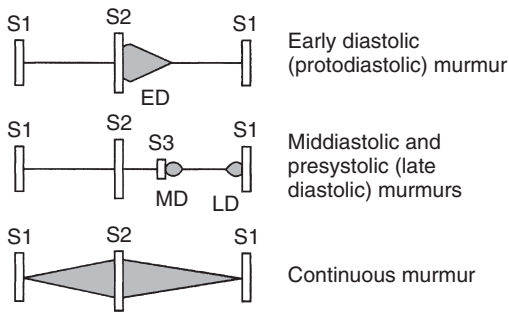


FIGURE 1-8
Diastolic murmurs and the continuous murmur. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

TABLE 1-8

COMMON INNOCENT HEART MURMURS

TYPE (TIMING)	DESCRIPTION OF MURMUR	AGE GROUP
Classic Vibratory Murmur (Still Murmur) (Systolic)	Maximal at MLSB or between LLSB and apex Grade 2-3/6 Low-frequency vibratory, twanging string, groaning, squeaking, or musical	3-6 yr Occasionally in infancy
Pulmonary Ejection Murmur (Systolic)	Maximal at ULSB Early to midsystolic Grade 1-3/6 in intensity Blowing in quality	8-14 yr
Pulmonary Flow Murmur of Newborn (Systolic)	Maximal at ULSB Transmits well to left and right chest, axillae, and back Grade 1-2/6 in intensity	Premature and full-term newborns Usually disappears by 3-6 mo of age
Venous Hum (Continuous)	Maximal at right (or left) supraclavicular and infraclavicular areas Grade 1-3/6 in intensity Audible only on sitting position (Inaudible in supine position) Intensity changes with rotation of head and compression of jugular vein	3-6 yr
Carotid Bruit (Systolic)	Right supraclavicular area and over carotids Grade 2-3/6 in intensity Occasional thrill over carotid	Any age

7. Innocent murmurs. Over 80% of children have innocent murmurs of one type or other sometime during childhood, most commonly beginning at about 3 or 4 years of age. All innocent heart murmurs are accentuated or brought out in high-output states, most importantly with fever. Clinical characteristics of these murmurs are summarized in [Table 1-8](#).
8. Pathologic murmurs. When one or more of the following are present, the murmur is likely to be pathologic and require cardiac consultation: (1) symptoms, (2) cyanosis, (3) abnormal chest radiography (heart size and/or silhouette and pulmonary vascularity), (4) abnormal ECG, (5) a systolic murmur that is loud (grade 3/6 or with a thrill) and long in duration, (6) a diastolic murmur, (7) abnormal heart sounds, and (8) abnormally strong or weak pulses.

Chapter 2

Electrocardiography

2

One normal cardiac cycle is represented by successive waveforms on an ECG tracing: the P wave, the QRS complex, and the T wave (Fig. 2-1, A). These waves produce two important intervals, PR and QT, and two segments, PQ and ST.

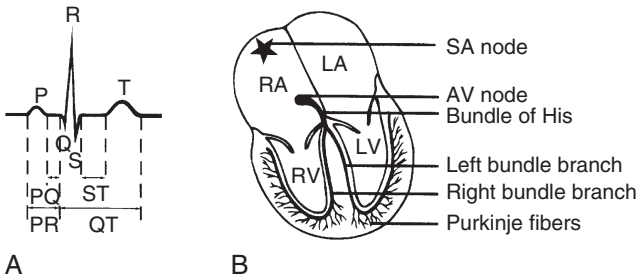
In normal sinus rhythm the sinoatrial (SA) node is the pacemaker for the entire heart; the SA node impulse depolarizes the right and left atria by a contiguous spread, producing the P wave (Fig. 2-1, A, B). When the atrial impulse arrives at the AV node, it passes through the node much more slowly than any other part of the heart, producing the PQ interval. Once the electrical impulse reaches the bundle of His, conduction becomes very fast and spreads simultaneously down the left and right bundle branches to the ventricular muscle through the Purkinje fibers, producing the QRS complex. The repolarization of the ventricle produces the T wave, but the repolarization of the atria is not usually visible on the ECG tracing. The ST segment represents phase 2 (plateau) of the action potential during which no net ionic movement occurs because the outward current (carried by K^+ and Cl^- ions) and inward current (carried by Ca^{2+} ions) are in competition.

A. Vectorial Approach to the ECG

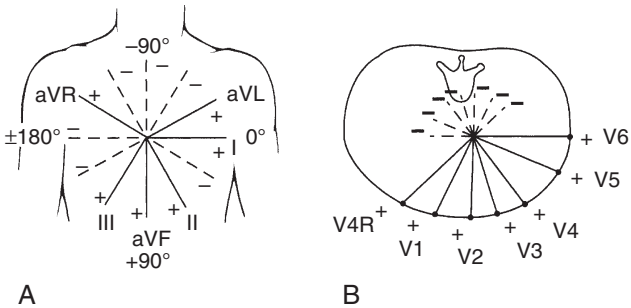
A scalar ECG, which is routinely obtained in clinical practice, shows only the magnitude of the forces against time. The vectorial approach views the standard scalar ECG as three-dimensional vector forces that vary with time. When leads, which represent the frontal and horizontal projection, are combined, one can derive three-dimensional information on the direction of the electromotive force from scalar ECG. The limb leads (i.e., leads I, II, III, aVR, aVL, and aVF) provide information about the frontal projection, while the precordial leads (V4R, and V1 through V6) provide information about the horizontal plane (Fig. 2-2). The vectorial approach clarifies the meaning of the ECG waves and the concept of axes, such as the P axis, QRS axis, and T axis. It is important for the readers to become familiar with the orientation of each scalar ECG lead.

1. The hexaxial reference system.

The *hexaxial reference system* is composed of six limb leads (leads I, II, III, aVR, aVL, and aVF). It gives information about the left-right and superior-inferior relationships (Fig. 2-2, A). The positive pole of each lead is indicated by the lead labels (and + signs). The positive deflection (i.e., the R wave) is the force directed toward the positive pole, and the negative deflection (i.e., the S wave) is the force directed toward the negative pole. Therefore, the R wave in lead I represents the leftward force and the S wave in lead I the rightward force. The R wave in aVF

**FIGURE 2-1**

A, Definition of ECG configuration and **B**, diagrammatic representation of the conduction system of the heart. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, 2006, Mosby.)

**FIGURE 2-2**

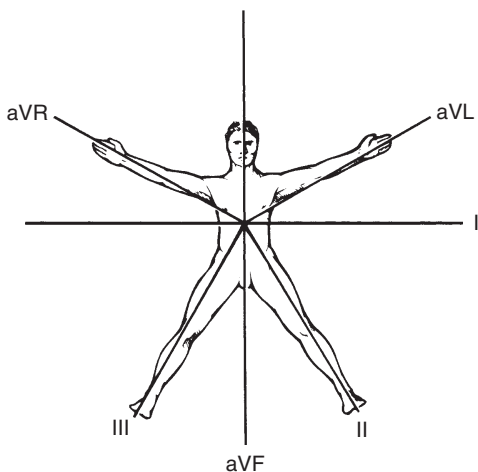
A, Hexaxial reference system. **B**, Horizontal reference system. (Adapted from Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

is the inferior force, and the S wave in the same lead represents the superior force. The R wave in lead II is the left and inferior force, and the R wave in lead III is the right and inferior force.

An easy way to memorize the hexaxial reference system is shown in Figure 2-3 by a superimposition of a body with stretched arms and legs on the X and Y axes. The hands and feet are the positive poles of certain leads. The left and right hands are the positive poles of leads aVL and aVR, respectively. The left and right feet are the positive poles of leads II and III, respectively. The bipolar limb leads I, II, and III are clockwise in sequence for the positive poles.

2. The horizontal reference system.

The *horizontal reference system*, on the other hand, gives information about the anteroposterior and left-right relationships. The horizontal reference system uses precordial leads (e.g., V4R, V1, V2, V5, and V6) (Fig. 2-2, B). The positive poles of the precordial leads are marked by

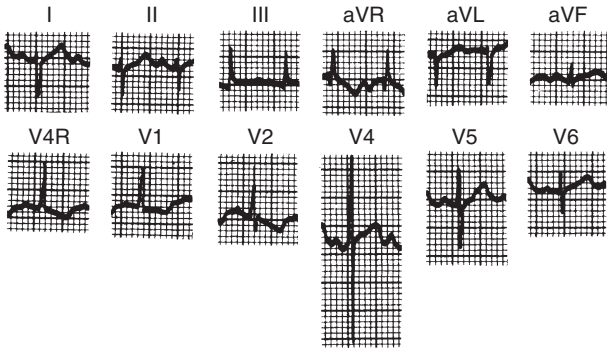
**FIGURE 2-3**

Easy way to memorize the hexaxial reference system.

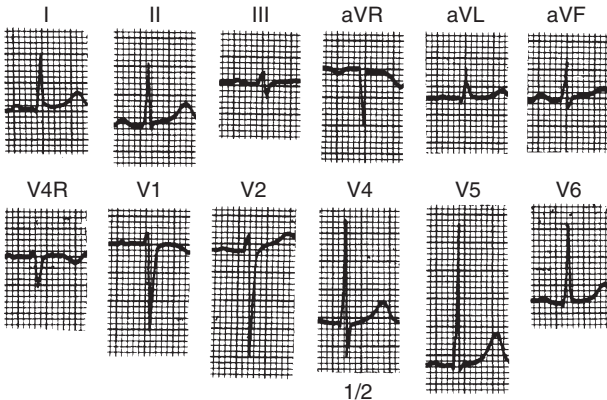
the lead labels. The R wave in V2 represents the anterior force and the S wave in the same lead represents the posterior force. The R wave in V6 is the leftward force and the S wave in the same lead is the rightward force. The R wave in V1 (as well as in V4R) is the right and anterior force and the S wave in this lead is the posterior and leftward force. The V4R lead is very useful in pediatrics; the position of the V4R lead is in the right chest at the mirror image position of the V4 lead.

B. Normal Pediatric Electrocardiograms

1. ECGs of normal infants and children are different from those of normal adults. The RV dominance seen in the ECG of neonates and infants is the result of the fetal circulation. The RV dominance is most marked in the neonate and is gradually replaced by the LV dominance of later childhood and adulthood.
2. By age 3 to 4 years, pediatric ECGs resemble those of the adult. [Figures 2-4 and 2-5](#) are ECGs from a newborn and an adult, respectively.
3. The pediatric ECG has the following characteristics:
 - a. The heart rate is faster than in the adult.
 - b. All the durations and intervals (PR interval, QRS duration, and QT interval) are shorter than in the adult.
 - c. The RV dominance of the neonate and infant is expressed in the ECG by the following:
 - (1) RAD is usually present.
 - (2) Large rightward forces (tall R waves in aVR and the right precordial leads [RPLs, i.e., V4R, V1, and V2] and deep S waves in lead I and the left precordial leads [LPLs, i.e., V5 and V6]).

**FIGURE 2-4**

ECG of a normal newborn infant.

**FIGURE 2-5**

ECG of a normal young adult.

- (3) The R/S ratios in the RPLs are large and those in the LPLs are small. The R/S ratio is the ratio of the R amplitude and the S amplitude in a given lead.
- d. The T wave is inverted in V1 in infants and small children with the exception of the first 3 days when the T waves may be normally upright.

C. Routine Interpretation

The following sequence is one of many approaches that can be used in routine interpretation of an ECG.

- Rhythm (sinus or nonsinus), considering the P axis.
- Heart rate (atrial and ventricular rates, if different).

- The QRS axis, the T axis, and the QRS-T angle.
- Intervals and duration: PR, QRS, and QT.
- The P wave amplitude and duration.
- The QRS amplitude and R/S ratio; also note abnormal Q waves.
- ST segment and T wave abnormalities.

1. Rhythm

- Definition of sinus rhythm. Sinus rhythm is the normal rhythm at any age. It must meet the following two characteristics (Fig. 2-6, A).
 - (1) A P wave preceding each QRS complex with a regular PR interval. (The PR interval may be prolonged as in first-degree AV block.)
 - (2) The P axis between 0 and +90 degrees (with upright P waves in leads I and aVF).
- The ECG of sinus rhythm. Because the sinoatrial (SA) node is located in the right upper part of the atrial mass, the direction of atrial depolarization is from the right upper part toward the left lower part, with the resulting P axis in the left lower quadrant (0 to +90 degrees) (Fig. 2-6, A). For the P axis to be between 0 and +90 degrees, P waves must be upright in leads I and aVF (Fig. 2-7, A). P waves may be flat but they should not be inverted in these two leads.
- Nonsinus rhythm. Even when there are P waves in front of the QRS complexes, if the P axis is not in the left lower quadrant (0 to +90 degrees), the cardiac rhythm is not sinus rhythm. Examples of nonsinus rhythm are shown in Figures 2-6, B, and 2-7, B. The P axis is in the left upper quadrant in Figure 2-6, B, with upright P waves in lead

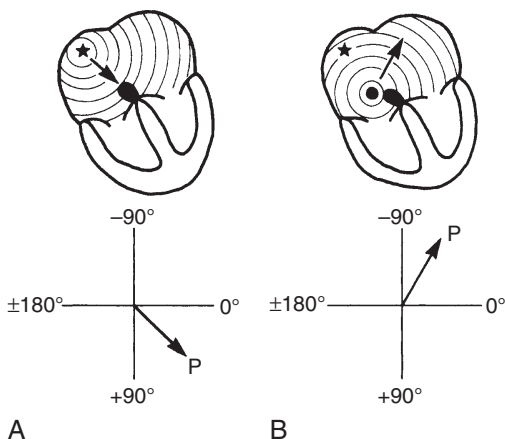


FIGURE 2-6

Comparison of P axis in sinus rhythm (**A**) and nonsinus rhythm or low atrial rhythm (**B**). In sinus rhythm, the P axis is between 0 and +90 degrees, and in nonsinus rhythm, the P axis is out of the 0 to +90-degree quadrant.

I and inverted P waves in a VF in [Figure 2-7, B](#). The rhythm in this case is called “low atrial rhythm” or “coronary sinus rhythm.”

2. Heart rate. At the usual paper speed of 25 mm/sec, 1 mm = 0.04 sec and 5 mm = 0.2 sec.
 - a. The heart rate may be calculated by dividing 60 (seconds) by the RR interval in seconds.
 - b. For quick estimation, inspect the RR interval in millimeters and use the following relationship: 5 mm, 300/sec; 10 mm, 150/sec; 15 mm, 100/sec; 20 mm, 75/sec; 25 mm, 60/sec ([Fig. 2-8](#)).
 - c. Normal resting heart rates per minute according to age are shown in [Table 2-1](#). Tachycardia is a heart rate faster than the upper range of

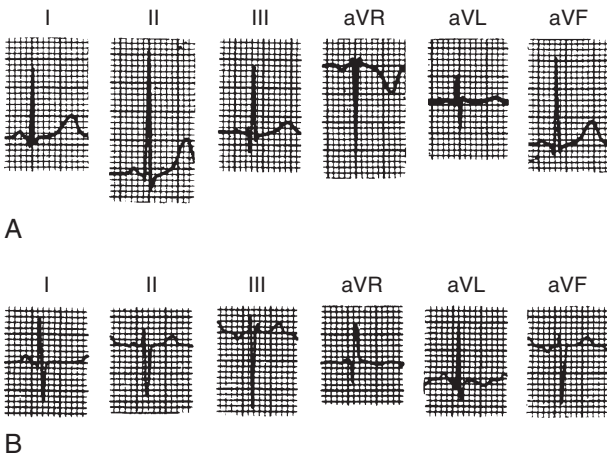


FIGURE 2-7

Sinus or nonsinus rhythm determined by the P axis. **A**, Sinus rhythm with the P axis between 0 and +90 degrees. **B**, A nonsinus rhythm with the P axis in the 0 to -90-degree quadrant.

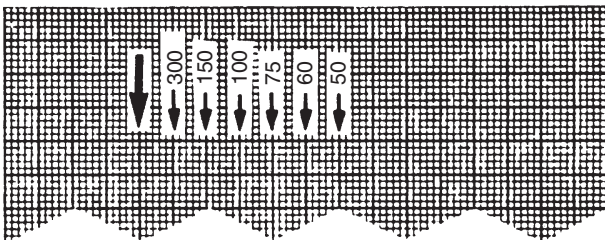


FIGURE 2-8

Quick method of estimating heart rate.

TABLE 2-1
NORMAL RANGES OF RESTING HEART RATE

AGE	BEATS/MIN
Neonates	110-150
2 yr	85-125
4 yr	75-115
Over 6 yr	60-100

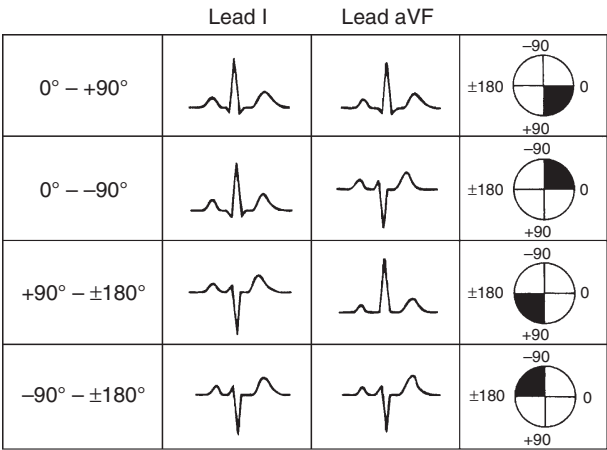
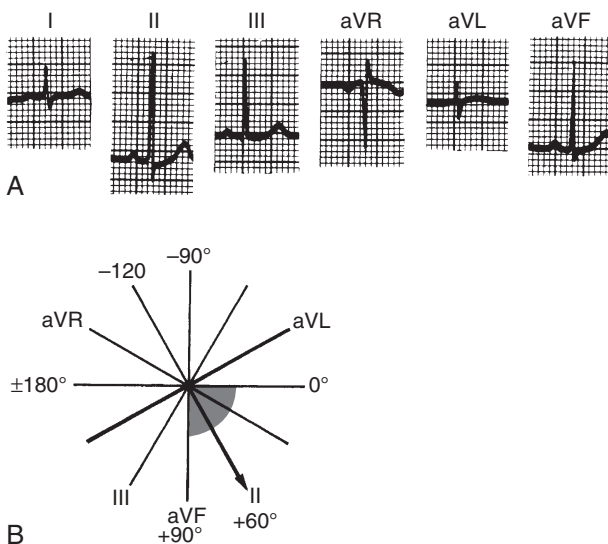


FIGURE 2-9
Locating quadrants of the QRS axis using leads I and aVF. This figure is also used in determining the P and T axes. In the *top panel*, the QRS complexes are upright in both leads I and aVF and thus the axis is in the 0 to +90 degrees quadrant. The P and T waves are also upright in leads I and aVF, and thus, the P and T axes are in the left lower quadrant (0 to +90 degrees) as well. The P axis in this quadrant indicates a sinus rhythm. The normal T axis is always in the left lower quadrant (0 to +90 degrees) at any age. Using the similar approaches, the QRS axis can be located for other panels. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

normal, and bradycardia is a heart rate slower than the low range of normal for that age.

- 3. The QRS axis, the T axis, and the QRS-T angle
 - a. **Successive approximation method.** A convenient way of determining the QRS axis is by the use of the hexaxial reference system (see Fig. 2-2, A).
 - (1) Step 1. Locate a quadrant using leads I and aVF (Fig. 2-9).
 - (2) Step 2. Find a lead with equiphasic QRS complex (in which the height of the R wave and the depth of the S wave are equal).
The QRS axis is perpendicular to the lead with equiphasic QRS complex in the predetermined quadrant.
 - (3) **Example 1.** Determine the QRS axis in Figure 2-10, A.

**FIGURE 2-10**

An example of a QRS axis determination using the successive approximation method. The six limb leads shown at the top (**A**) are from a 6-year-old child. The QRS axis is plotted in a hexaxial reference system (**B**) (see text).

- (a) Step 1. The axis is in the left lower quadrant (0 to +90 degrees), since the R waves are upright in leads I and aVF.
- (b) Step 2. The QRS complex is equiphasic in aVL. Therefore, the QRS axis is +60 degrees, which is perpendicular to aVL (Fig. 2-10, B).
- (4) **Example 2.** Determine the QRS axis in Figure 2-11, A.
 - (a) Step 1. The QRS complexes are negative in lead I and negative in aVF, placing the axis in the right upper quadrant (−90 to −180 degrees) (see bottom panel of Fig. 2-9).
 - (b) Step 2. It is almost equiphasic in aVL. Therefore, the axis is close to −120 degrees. The QRS axis in the right upper quadrant is called *indeterminate*, that is, neither right nor left.
- b. The QRS axis.
 - (1) The normal QRS axis varies with age (see Table 2-2).
 - (2) The abnormal QRS axis has the following significance:
 - (a) LAD (with the QRS axis less than the lower limits of normal) is seen in LVH, LBBB, and left anterior hemiblock (or superior QRS axis, characteristically seen with endocardial cushion defect [ECD] and tricuspid atresia).
 - (b) RAD (with the QRS axis greater than the upper limits of normal) is seen in RVH and RBBB.

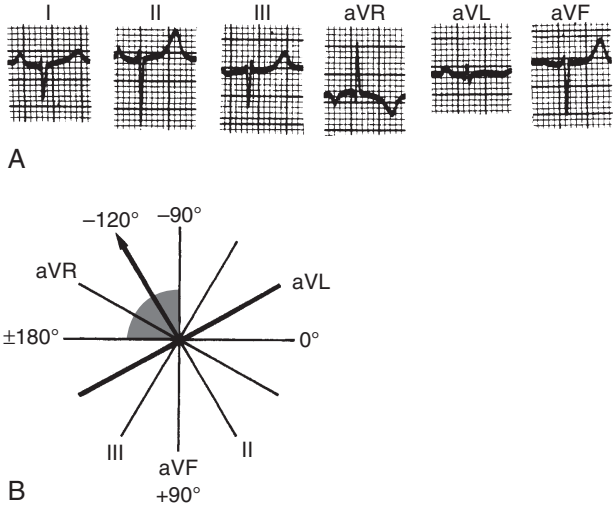


FIGURE 2-11

An example of a QRS axis determination using the successive approximation method. The six limb leads shown at the top **(A)** are from a 2-year-old child with Down syndrome. The QRS axis is plotted in a hexaxial reference system **(B)** (see text).

TABLE 2-2

MEAN AND RANGE OF NORMAL QRS AXES

1 wk–1 mo	+110 degrees (+30 to +180)
1–3 mo	+ 70 degrees (+10 to +125)
3 mo–3 yr	+ 60 degrees (+10 to +110)
>3 yr	+ 60 degrees (+20 to +120)
Adults	+ 50 degrees (–30 to +105)

- (c) A superior QRS axis is present when the S wave is greater than the R wave in aVF. It includes the left anterior hemiblock (in the range of –30 degrees to –90 degrees) and extreme RAD.
- c. The T axis can be determined by the same method as that used to determine the QRS axis.
- (1) **Examples.** Determine the T axis in [Figure 2-11, A](#).
- (a) In [Figure 2-11, A](#), the positive T wave in lead I and the positive T wave in aVF place the T axis in the left lower quadrant (0 to +90 degrees).
- (b) The T wave is nearly flat in aVL, and therefore the T axis is perpendicular to this lead, close to +60 degrees (or the positive pole of lead II, which shows the tallest T wave).
- (2) The normal T axis is 0 to +90 degrees.
- (3) The abnormal T axis (outside the 0 to +90-degree quadrant) is present when the T wave is inverted in lead I or aVF (usually

resulting in a wide QRS-T angle). An abnormal T axis suggests conditions with abnormal myocardial repolarization (myocarditis, myocardial ischemia), ventricular hypertrophy with strain, or RBBB.

- d. The QRS-T angle is the angle formed by the QRS axis and the T axis. In [Figure 2-11](#), the QRS-T angle is about 180 degrees (because the QRS axis is -120 degrees, and the T axis is about $+60$ degrees).

- (1) The normal QRS-T angle is less than 60 degrees except in the newborn period, when it may be more than 60 degrees.
- (2) The QRS-T angle of more than 60 degrees is unusual and that of more than 90 degrees is certainly abnormal. The abnormal QRS-T angle (above 90 degrees) is seen in severe ventricular hypertrophy with strain, ventricular conduction disturbances, ventricular arrhythmias, and myocardial dysfunction of a metabolic or ischemic nature.

4. Intervals

- a. **The PR interval.** The PR interval is measured from the onset of the P wave to the beginning of the QRS complex.
 - (1) The normal PR interval varies with age and heart rate ([Table 2-3](#)). The older the person and the slower the heart rate, the longer the PR interval.
 - (2) A prolonged PR interval (first-degree AV block) may be seen in myocarditis (viral, rheumatic, or diphtheric), digitalis or quinidine toxicity, certain CHDs (ECD, ASD, Ebstein anomaly), hyperkalemia, other myocardial dysfunction, and in otherwise normal hearts.
 - (3) A short PR interval is present in Wolff-Parkinson-White (WPW) pre-excitation, Lown-Ganong-Levine preexcitation, Duchenne muscular dystrophy (or relatives of these patients), Friedreich ataxia, pheochromocytoma, glycogen storage disease, and otherwise normal children.
 - (4) Variable PR intervals are seen in wandering atrial pacemaker and Wenckebach (Mobitz type I) second-degree AV block.
- b. **The QRS duration.** Normal QRS duration varies with age and is shorter in infants and children than in adults ([Table 2-4](#)).
 - (1) A prolonged QRS is characteristic of ventricular conduction disturbances, which include bundle branch blocks (BBBs), WPW preexcitation, and intraventricular block. (See later section: "Ventricular Conduction Disturbances").
 - (2) A slight prolongation of the QRS duration may also be seen in ventricular hypertrophy.
- c. **The QT interval.** The QT interval normally varies primarily with heart rate. The heart rate-corrected QT interval (QTc) can be calculated with Bazett formula:

$$QTc = QT / \sqrt{RR \text{ interval}}$$

- (1) According to Bazett formula, the normal QTc interval (mean \pm SD) is $0.40 (\pm 0.014)$ seconds with the upper limit of normal 0.44 seconds in children 6 month and older.

TABLE 2-3

PR INTERVAL WITH RATE AND AGE (UPPER LIMITS OF NORMAL)

RATE	0-1 MO	1-6 MO	6 MO-1 YR	1-3 YR	3-8 YR	8-12 YR	12-16 YR	ADULT
<60						0.16 (0.18)	0.16 (0.19)	0.17 (0.21)
60-80					0.15 (0.17)	0.15 (0.17)	0.15 (0.18)	0.16 (0.21)
80-100	0.10 (0.12)				0.14 (0.16)	0.15 (0.16)	0.15 (0.17)	0.15 (0.20)
100-120	0.10 (0.12)			(0.15)	0.13 (0.16)	0.14 (0.15)	0.15 (0.16)	0.15 (0.19)
120-140	0.10 (0.11)	0.11 (0.14)	0.11 (0.14)	0.12 (0.14)	0.13 (0.15)	0.14 (0.15)		0.15 (0.18)
140-160	0.09 (0.11)	0.10 (0.13)	0.11 (0.13)	0.11 (0.14)	0.12 (0.14)			(0.17)
160-180	0.10 (0.11)	0.10 (0.12)	0.10 (0.12)	0.10 (0.12)				
>180	0.09	0.09 (0.11)	0.10 (0.11)					

From Park MK, Guntheroth WG: How to Read Pediatric ECGs, ed 4, Philadelphia, 2006, Mosby.

TABLE 2-4

QRS DURATION ACCORDING TO AGE: MEAN (UPPER LIMITS OF NORMAL*) (IN SECONDS)

	0-1 MO	1-6 MO	6-12 MO	1-3 YR	3-8 YR	8-12 YR	12-16 YR	ADULTS
Seconds	0.05 (0.07)	0.055 (0.075)	0.055 (0.075)	0.055 (0.075)	0.06 (0.075)	0.06 (0.085)	0.07 (0.085)	0.08 (0.10)

*Upper limit of normal refers to the 98th percentile.

Derived from percentile charts in Davignon A, Rautaharju P, Boisselle E, et al. Normal ECG Standards for Infants and Children. Pediatric Cardiology 1:123-131, 1979/80

- (2) The QTc interval is slightly longer in the newborn and small infants with the upper limit of normal QTc 0.47 seconds in the first week of life and 0.45 seconds in the first 6 months of life.
- (3) Prolonged QT intervals predispose to serious ventricular arrhythmias.
 - (a) Prolonged QT intervals may be seen in long QT syndrome (e.g., Jervell and Lange-Nielsen syndrome, Romano-Ward syndrome), hypocalcemia, myocarditis, diffuse myocardial diseases (including hypertrophic and dilated cardiomyopathies), head injury, severe malnutrition, and so on.
 - (b) A number of drugs are also known to prolong the QT interval. Among these are antiarrhythmic agents (especially class IA, IC, and III), antipsychotic phenothiazines (e.g., thioridazine, chlorpromazine), tricyclic antidepressants (e.g., imipramine, amitriptyline), arsenics, organophosphates, antibiotics (e.g., azithromycin, erythromycin, trimethoprim-sulfa, amantadine), and antihistamines (e.g., terfenadine) (see Box 16-1, Acquired Causes of QT Prolongation).
- (4) Short QT intervals can also predispose to serious ventricular arrhythmias.
 - (a) Short QT interval is seen with hypocalcemia or hyperthermia. It is also a sign of a digitalis effect.
 - (b) Short QT syndrome (in which the QTc is ≤ 300 milliseconds) is a familial cause of sudden death by ventricular tachycardia.
- d. **The JT interval.** The JT interval is useful when the QT interval is prolonged secondary to a prolonged QRS duration. It is measured from the J point (the junction between the S wave and the ST segment) to the end of the T wave. The JT interval is also expressed as a rate-corrected interval (called JTc) using Bazett formula. A prolonged JT interval has the same significance as the prolonged QTc interval. Normal JTc (mean \pm SD) is 0.32 ± 0.02 seconds with the upper limit of normal 0.34 seconds.
5. P wave duration and amplitude. Abnormal amplitude or duration indicates atrial hypertrophy.
 - a. Normally the P wave amplitude is less than 3 mm. Tall P waves indicate RAH.
 - b. The duration of the P waves is shorter than 0.09 seconds in children and shorter than 0.07 seconds in infants. Long P wave durations are seen in LAH.
6. QRS amplitude, R/S ratio, and abnormal Q waves
 - a. QRS amplitude varies with age (Tables 2-5 and 2-6).
 - (1) Large QRS amplitudes (either large R waves or deep S waves) are found in ventricular hypertrophy and ventricular conduction disturbances (e.g., BBBs, WPW preexcitation).
 - (2) Low QRS voltages are seen in pericarditis, myocarditis, hypothyroidism, and normal neonates.

TABLE 2-5

R VOLTAGES ACCORDING TO LEAD AND AGE: MEAN (AND UPPER LIMIT*) (IN MM)

	0–1 MO	1–6 MO	6–12 MO	1–3 YR	3–8 YR	8–12 YR	12–16 YR	ADULTS
I	4 (8)	7 (13)	8 (16)	8 (16)	7 (15)	7 (15)	6 (13)	6 (13)
II	6 (14)	13 (24)	13 (27)	12 (23)	13 (22)	14 (24)	14 (24)	5 (25)
III	8 (16)	9 (20)	9 (20)	9 (20)	9 (20)	9 (24)	9 (24)	6 (22)
aVR	3 (8)	2 (6)	2 (6)	2 (5)	2 (4)	1 (4)	1 (4)	1 (4)
aVL	2 (7)	4 (8)	5 (10)	5 (10)	3 (10)	3 (10)	3 (12)	3 (9)
aVF	7 (14)	10 (20)	10 (16)	8 (20)	10 (19)	10 (20)	11 (21)	5 (23)
V3R	10 (19)	6 (13)	6 (11)	6 (11)	5 (10)	3 (9)	3 (7)	
V4R	6 (12)	5 (10)	4 (8)	4 (8)	3 (8)	3 (7)	3 (7)	
V1	13 (24)	10 (19)	10 (20)	9 (18)	8 (16)	5 (12)	4 (10)	3 (14)
V2	18 (30)	20 (31)	22 (32)	19 (28)	15 (25)	12 (20)	10 (19)	6 (21)
V5	12 (23)	20 (33)	20 (31)	20 (32)	23 (38)	26 (39)	21 (35)	12 (33)
V6	5 (15)	13 (22)	13 (23)	13 (23)	15 (26)	17 (26)	14 (23)	10 (21)

*Upper limit of normal refers to the 98th percentile.

Voltages measured in millimeters, when 1 mV = 10 mm paper.

Data are from Park MK, Guntheroth WG, How to Read Pediatric ECGs, ed 4, Philadelphia, 2006, Mosby.

TABLE 2-6

S VOLTAGES ACCORDING TO LEAD AND AGE: MEAN (AND UPPER LIMIT*) (IN MM)

	0–1 MO	1–6 MO	6–12 MO	1–3 YR	3–8 YR	8–12 YR	12–16 YR	ADULTS
I	5 (10)	4 (9)	4 (9)	3 (8)	2 (8)	2 (8)	2 (8)	1 (6)
V3R	3 (12)	3 (10)	4 (10)	5 (12)	7 (15)	8 (18)	7 (16)	
V4R	4 (9)	4 (12)	5 (12)	5 (12)	5 (14)	6 (20)	6 (20)	
V1	7 (18)	5 (15)	7 (18)	8 (21)	11 (23)	12 (25)	11 (22)	10 (23)
V2	18 (33)	15 (26)	16 (29)	18 (30)	20 (33)	21 (36)	18 (33)	14 (36)
V5	9 (17)	7 (16)	6 (15)	5 (12)	4 (10)	3 (8)	3 (8)	
V6	3 (10)	3 (9)	2 (7)	2 (7)	2 (5)	1 (4)	1 (4)	1 (13)

*Upper limit of normal refers to the 98th percentile.

Voltages measured in millimeters, when 1 mV = 10 mm paper.

Data are from Park MK, Guntheroth WG, How to Read Pediatric ECGs, ed 4, Philadelphia, 2006, Mosby.

- b. The R/S ratio in normal infants and small children is large in the right precordial leads (RPLs) and is small in the left precordial leads (LPLs) because of the presence of tall R waves in the RPLs and deep S waves in the LPLs (Table 2-7). Abnormal R/S ratios are seen in ventricular hypertrophy and ventricular conduction disturbances.
- c. Normal Q waves are narrow (0.02 seconds) and are usually less than 5 mm in LPLs and aVF (Table 2-8). They may be as deep as 8 mm in lead III in children younger than 3 years old.
 - (1) Deep Q waves may be present in the LPLs in LVH of volume overload type.
 - (2) Deep and wide Q waves are seen in myocardial infarction and myocardial fibrosis.
 - (3) Q waves are normally absent in RPLs.

TABLE 2-7

R/S RATIO ACCORDING TO AGE: MEAN, LOWER, AND UPPER LIMITS OF NORMAL

	LEAD	0-1 MO	1-6 MO	6 MO-1 YR	1-3 YR	3-8 YR	8-12 YR	12-16 YR	ADULT
V1	LLN	0.5	0.3	0.3	0.5	0.1	0.15	0.1	0.0
	Mean	1.5	1.5	1.2	0.8	0.65	0.5	0.3	0.3
	ULN	19	S = 0	6	2	2	1	1	1
V2	LLN	0.3	0.3	0.3	0.3	0.05	0.1	0.1	0.1
	Mean	1	1.2	1	0.8	0.5	0.5	0.5	0.2
	ULN	3	4	4	1.5	1.5	1.2	1.2	2.5
V6	LLN	0.1	1.5	2	3	2.5	4	2.5	2.5
	Mean	2	4	6	20	20	20	10	9
	ULN	S = 0	S = 0	S = 0	S = 0	S = 0	S = 0	S = 0	S = 0

LLN, lower limit of normal; ULN, upper limit of normal.

From Guntheroth WG: Pediatric Electrocardiography, Philadelphia, WB Saunders, 1965.

TABLE 2-8

Q VOLTAGES ACCORDING TO LEAD AND AGE: MEAN (AND UPPER LIMIT*) (IN MM)

	0-1 MO	1-6 MO	6-12 MO	1-3 YR	3-8 YR	8-12 YR	12-16 YR	ADULTS
III	1.5 (5.5)	1.5 (6.0)	2.1 (6.0)	1.5 (5.0)	1.0 (3.5)	0.6 (3.0)	1.0 (3.0)	0.5 (4)
aVF	1.0 (3.5)	1.0 (3.5)	1.0 (3.5)	1.0 (3.0)	0.5 (3.0)	0.5 (2.5)	0.5 (2.0)	0.5 (2)
V5	0.1 (3.5)	0.1 (3.0)	0.1 (3.0)	0.5 (4.5)	1.0 (5.5)	1.0 (3.0)	0.5 (3.0)	0.5 (3.5)
V6	0.5 (3.0)	0.5 (3.0)	0.5 (3.0)	0.5 (3.0)	1.0 (3.5)	0.5 (3.0)	0.5 (3.0)	0.5 (3)

*Upper limit of normal refers to the 98th percentile.

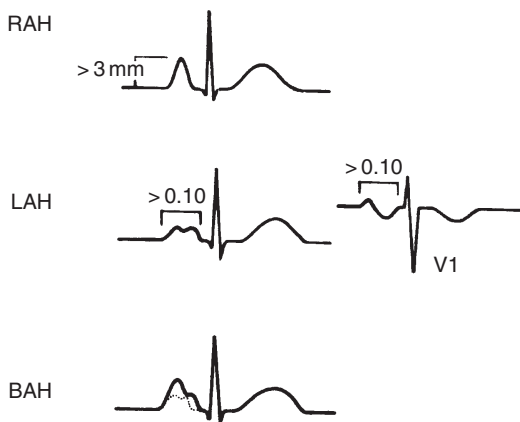
Voltages measured in millimeters, when 1 mV = 10 mm paper.

Data are from percentile charts in Davignon A, Rautaharju P, Boisselle E, et al., Normal ECG Standards for Infants and Children, Pediatric Cardiology 1:123-131, 1979/80.

- (a) Q waves in V1 may be seen in ventricular inversion (L-TGA), severe RVH, single ventricle, and occasional neonates.
- (b) Absent Q waves in V6 may be seen in LBBB and ventricular inversion.

7. The ST segment and the T wave

- a. The normal ST segment is isoelectric. Some forms of ST segment shifts are nonpathologic and they include J depression and early repolarization. Pathologic ST segment shift may assume either a downward sloping or a sustained horizontal depression and is seen with myocarditis, pericarditis, and myocardial ischemia or infarction. A further discussion follows later in this chapter.
- b. The T wave
 - (1) Normal T axis should be in the left lower quadrant (0 to +90 degrees).
 - (2) Tall peaked T waves may be seen in hyperkalemia, LVH (volume overload), and cerebrovascular accident.
 - (3) Flat or low T waves may occur in normal neonates or with such conditions as hypothyroidism, hypokalemia, pericarditis, myocarditis, myocardial ischemia, hyperglycemia, or hypoglycemia.

**FIGURE 2-12**

Criteria for atrial hypertrophy. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

D. Atrial Hypertrophy

Abnormalities in the P wave amplitude and/or duration characterize atrial hypertrophy (see Fig. 2-12).

1. Right atrial hypertrophy (RAH) accompanies tall P waves (at least 3 mm).
2. Left atrial hypertrophy (LAH) accompanies wide P wave duration (at least 0.1 seconds in children and >0.08 seconds in infants). A biphasic P wave in V1 is not a sign of LAH, unless the P wave duration is greater than 0.08 seconds for infants and greater than 0.1 second for children.
3. Biatrial hypertrophy (BAH) accompanies a combination of tall and wide P waves.

E. Ventricular Hypertrophy

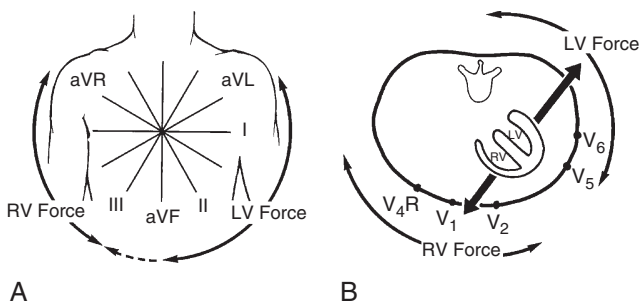
1. Ventricular hypertrophy produces abnormalities in one or more of the following: the QRS axis, the QRS voltages, the R/S ratio, the T axis, and miscellaneous changes.

- a. The QRS axis is usually directed toward the hypertrophied ventricle (see Table 2-2 for the normal QRS axis).

(1) RAD is seen with RVH.

(2) LAD is seen with LVH. However, LAD is rare with LVH caused by pressure overload; in this situation, the QRS axis is more often directed inferiorly.

- b. Changes in QRS voltages. Anatomically, the RV occupies the right and anterior aspect, and the LV occupies the left, inferior, and posterior aspect of the ventricular mass. With ventricular hypertrophy, the voltage of the QRS complex increases in the direction of the respective ventricle (see Tables 2-5 and 2-6 for normal R and S voltages).

**FIGURE 2-13**

Left and right ventricular forces on the frontal (**A**) and horizontal (**B**) projections.

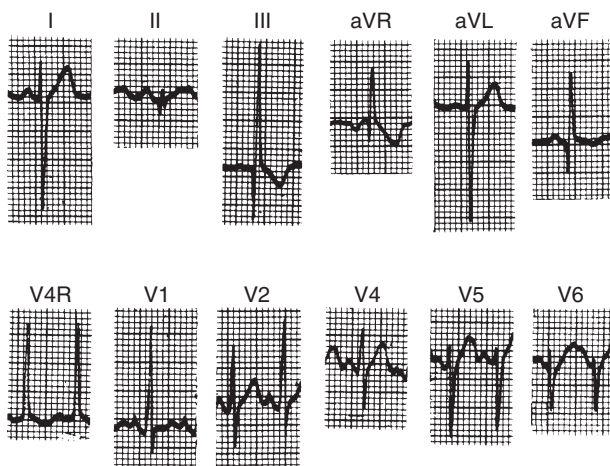
A, Hexaxial reference system. **B**, Horizontal plane. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

- (1) In the frontal plane (Figure 2-13, A),
 - (a) LVH shows increased R voltages in leads I, II, aVL, aVF, and sometimes III, especially in small infants.
 - (b) RVH shows increased R voltages in aVR and III and increased S voltages in lead I
- (2) In the horizontal plane (Figure 2-13, B),
 - (a) LVH shows tall R waves in V5 and V6 and/or deep S waves in V4R, V1, and V2.
 - (b) RVH shows tall R waves in V4R, V1, and V2 and/or deep S waves in V5 and V6.
- c. Changes in R/S ratio. An increase in the R/S ratio in the RPLs suggests RVH, and a decrease in the ratio in these leads suggests LVH. An increase in the R/S ratio in the LPLs suggests LVH and a decrease in the ratio suggests RVH (Table 2-7).
- d. Changes in the T axis. In severe ventricular hypertrophy with relative ischemia of the hypertrophied myocardium, the T axis changes. In the presence of criteria of ventricular hypertrophy, a wide QRS-T angle (90 degrees or greater) with the T axis outside the normal range indicates a strain pattern. When the T axis remains in the normal quadrant (0 to +90 degrees), a wide QRS-T angle indicates a possible strain pattern.
- e. Miscellaneous nonspecific changes
 - (1) RVH
 - (a) An upright T wave in V1 after 3 days of age is a sign of probable RVH.
 - (b) A Q wave in V1 (either qR or qRs) suggests RVH, although it may be present in ventricular inversion.
 - (2) LVH
 - (a) Deep Q waves (≥ 5 mm) and/or tall T waves in V5 and V6 are signs of LVH of the volume overload type (often seen with a large-shunt VSD).

- (b) Deep Q waves seen in the inferior leads (II, III, and aVF) may also be a sign of LVH (dilated or hypertrophied LV). Normally, the Q wave in lead III may be as deep as 6 mm in small children.

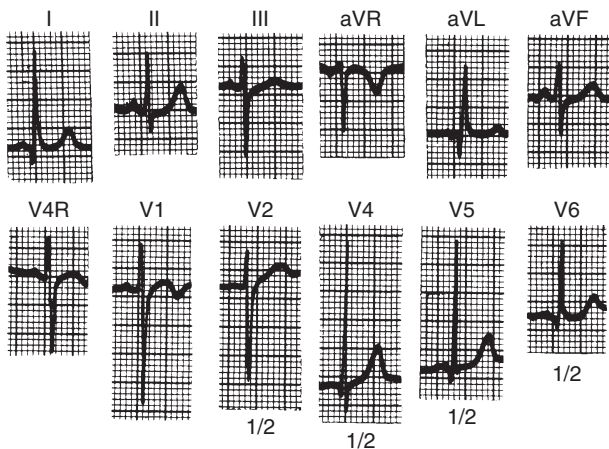
2. Criteria for RVH

- a. RAD for the patient's age (see [Table 2-2](#)).
 - b. Increased rightward and anterior QRS voltages in the presence of normal QRS duration. Increased QRS voltages in the presence of a prolonged QRS duration indicate a ventricular conduction disturbance, such as BBB or WPW preexcitation, rather than ventricular hypertrophy.
 - (1) R in V1, V2, or aVR greater than the upper limits of normal for the patient's age (see [Table 2-5](#)).
 - (2) S in I and V6 greater than the upper limits of normal for the patient's age (see [Table 2-6](#)).
 - c. Abnormal R/S ratio ([Table 2-7](#)).
 - (1) R/S ratio in V1 and V2 greater than the upper limits of normal for age.
 - (2) R/S ratio in V6 less than 1 after 1 month of age.
 - d. Upright T wave in V1 in patients more than 3 days of age, provided that the T is upright in the LPLs (V5, V6). Upright T in V1 is not abnormal in patients 6 years or older.
 - e. A Q wave in V1 (qR or qRs pattern) may be seen with severe RVH. (It is more likely ventricular inversion.)
 - f. In the presence of RVH, a wide QRS-T angle (≥ 90 degrees) with the T axis outside the normal range (usually in the 0- to -90 -degree quadrant) indicates a "strain" pattern.
 - g. The more independent criteria for RVH that are satisfied, the more probable RVH is. An abnormal force both rightward and anterior is stronger evidence than one that is anterior only or rightward only. For example, large S waves seen in two leads, I and V6 (rightward forces), are not as strong as a large S wave seen in lead I and a large R wave seen in V2 (reflecting both rightward and anterior forces). An example of RVH with "strain" is shown in [Figure 2-14](#).
3. RVH in the newborn. The diagnosis of RVH in the neonate is particularly difficult because of the normal dominance of the RV during that period of life. The following clues, however, are helpful.
- a. S waves in lead I ≥ 12 mm.
 - b. R waves in aVR ≥ 8 mm.
 - c. The following abnormalities in V1 also suggest RVH.
 - (1) Pure R wave (with no S wave) in V1 greater than 10 mm.
 - (2) A qR pattern in V1 (also seen in 10% of healthy newborn infants).
 - (3) Upright T waves in V1 in neonates older than 3 days of age (with upright T in V6).
 - d. RAD greater than $+180$ degrees.
4. Criteria for LVH
- a. LAD for the patient's age (see [Table 2-2](#)).
 - b. QRS voltages in favor of the LV in the presence of normal QRS duration.

**FIGURE 2-14**

Tracing from a 10-month-old infant with severe TOF. The tracing shows RVH with strain. There is RAD (+150 degrees). The R waves in III (22 mm) and aVR (9 mm) and the S waves in I (19 mm) and V6 (8 mm) are abnormally large, indicating RVH. The R/S ratios in V1 and V2 are abnormally large, and the ratio in V6 is smaller than the LLN (see Table 2-7), also indicating RVH. The S wave is inverted in aVF, with a T axis of -10 degrees and a wide QRS-T angle (160 degrees).

- (1) R in I, II, III, aVL, aVF, V5, or V6 greater than the upper limits of normal for age (see Table 2-5).
- (2) S in V1 or V2 greater than the upper limits of normal for age (see Table 2-6).
- c. Abnormal R/S ratio: An R/S ratio in V1 and V2 less than the lower limits of normal for the patient's age (Table 2-7).
- d. Q in V5 and V6, 5 mm or more, coupled with tall symmetric T waves in the same leads (volume overload type).
- e. In the presence of LVH, a wide QRS-T angle (≥ 90 degrees) with the T axis outside the normal quadrant indicates a "strain" pattern. This is manifested by inverted T waves in lead I or aVF.
- f. The more of the preceding independent criteria satisfied, the more probable LVH is. For example, abnormal leftward forces seen in three leads (I, V5, and V6) are not as strong as the situation in which abnormal leftward force (e.g., deep S in I) is combined with abnormal posterior forces (deep S in V2) or abnormal inferior force (tall R in aVF or tall R in II). With obstructive lesions (e.g., AS), the abnormal force is more likely inferior (not showing LAD). With a volume overload (e.g., VSD), the abnormal force is more likely to the left (showing LAD). An example of LVH is shown in Figure 2-15.

**FIGURE 2-15**

Tracing from a 4-year-old boy with moderate VSD. The tracing shows LVH without strain pattern. The QRS axis is 0 degrees (LAD for age). The R waves in I (17 mm), aVL (12 mm), V5 (44 mm), and V6 (27 mm) are beyond the upper limits of normal, indicating abnormal LV force. The T axis (+50 degrees) is in the normal range. Note one-half standardization for some precordial leads.

5. Criteria for biventricular hypertrophy (BVH).

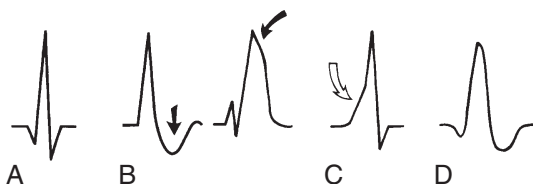
Diagnosis of BVH is often difficult because the abnormal LV and RV forces are opposite in direction and therefore tend to cancel out, resulting in relatively small (or even normal) QRS voltages.

- Positive voltage criteria for RVH and LVH in the absence of increased QRS duration (such as BBB or WPW preexcitation). Many cases of large QRS voltages suggestive of BVH are seen in ventricular conduction disturbances (with increased QRS duration).
- Positive voltage criteria for RVH or LVH and large voltages (but within normal limits) for the other ventricle, again in the presence of normal QRS duration.
- Large equiphasic QRS complexes in two or more of the limb leads and in the midprecordial leads (V2 through V5), called Katz-Wachtel phenomenon.

F. Ventricular Conduction Disturbances

Conditions that are grouped together as ventricular conduction disturbances have in common abnormal prolongation of QRS duration (Fig. 2-16). Three types of ventricular conduction disturbances and their characteristic findings are as follows.

- Right and left bundle branch blocks, in which the prolongation of the QRS duration is in the terminal portion of the QRS complex (i.e., “terminal slurring”) (Fig. 2-16, B).

**FIGURE 2-16**

Schematic diagram of three types of ventricular conduction disturbances. **A**, Normal QRS complex. **B**, QRS complexes in RBBB with terminal slurring (black arrows).

C, Preexcitation with delta wave (initial slurring, open arrow). **D**, Intraventricular block in which the prolongation of the QRS complex is throughout the duration of the QRS complex. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

- Wolff-Parkinson-White (WPW) preexcitation shows the prolongation in the initial portion of the QRS complex (i.e., initial slurring or delta wave) (Fig. 2-16, C).
- Intraventricular block in which the prolongation is throughout the QRS complex (Fig. 2-17, D).

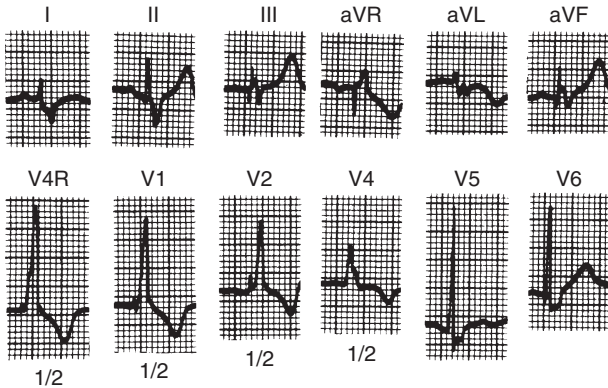
The normal QRS duration varies with age (see Table 2-4). In infants, QRS duration of 0.08 seconds (not 0.1, as in adults) meets the requirement for RBBB. Therefore, accurate determination of the QRS duration is necessary to diagnose ventricular conduction disturbances.

1. Right bundle branch block (RBBB)

- a. RBBB is the most common form of ventricular conduction disturbance in children.
- b. The RV depolarization is delayed with the terminal slurring of the QRS complex directed toward the RV (e.g., rightward and anteriorly). The RV depolarization is unopposed by the LV depolarization due to asynchronous depolarization of the opposing forces, and therefore the manifest QRS voltages are abnormally large, often a source of misinterpretation of the condition as ventricular hypertrophy. The same is the case with LBBB. Thus, larger QRS voltages for both the RV and the LV are seen in RBBB and LBBB. (Only RBBB will be presented here because LBBB is extremely rare in pediatric patients.)
- c. The two most common pediatric disorders that present with RBBB are ASD and conduction disturbances following heart surgery involving a right ventriculotomy. Other conditions often associated with RBBB include Ebstein anomaly, COA in infants less than 6 months of age, ECD, PAPVR, and occasionally in normal children.
- d. The significance of RBBB in children is different from that in adults. In several pediatric examples of RBBB, the right bundle is intact. In ASD, the prolonged QRS duration is the result of a longer pathway through a dilated RV, rather than an actual block in the right bundle. Right ventriculotomy for repair of VSD or tetralogy of Fallot disrupts

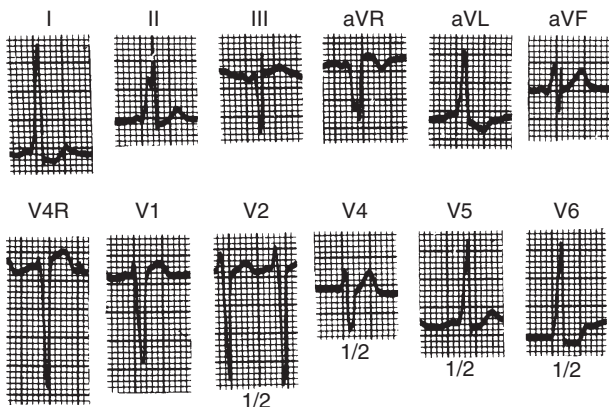
the RV subendocardial Purkinje network and causes prolongation of the QRS duration without necessarily injuring the right bundle.

- e. **RSR'** pattern. Although the RSR' (or rSr') pattern in V1 is unusual in adults, this pattern is a *normal* finding in infants, toddlers, and small children. Some of them are incorrectly interpreted as *incomplete right bundle branch block (IRBBB)* or RVH by computer readouts and by physicians alike. Looking at it from vectorcardiographic points of view, in order for a newborn ECG pattern to change to the adult pattern, it has to go through a stage in which the rSr' or RsR' pattern appears; it is almost impossible for a newborn ECG to change to the adult pattern without going through the rSr' (or rsR') stage. The following clarifies some issues related to the rSr' pattern in V1.
 - (1) An rsR' pattern in V1 is normal if the QRS duration and QRS voltage are normal.
 - (2) If the rSr' pattern is associated with slightly prolonged QRS duration (not to satisfy the criterion of RBBB), it is then incomplete RBBB. In this case, the QRS voltage could be slightly increased.
 - (3) If the rsR' pattern is associated with slightly prolonged QRS duration and an abnormally large QRS voltage, it is still IRBBB, not ventricular hypertrophy.
 - (4) RVH is justified only if an abnormal QRS voltage is present in the presence of normal QRS duration.
- f. **Incomplete right bundle branch block (IRBBB):** The pathophysiology and clinical significance of IRBBB are similar to that of RBBB as discussed above. Some cardiologists prefer the term "RV conduction delay" rather than a "block" as in IRBBB. The prevalence of IRBBB in the pediatric population is not known, but it may be around 1% among normal children and 5% to 10% in the adult population.
- g. **Criteria for RBBB (Fig. 2-17)**
 - (1) RAD at least for the terminal portion of the QRS complex. The initial QRS vector is normal.
 - (2) QRS duration longer than the upper limits of normal for the patient's age (see [Table 2-4](#)).
 - (3) Terminal slurring of the QRS complex directed to the right and usually, but not always, anteriorly.
 - (a) Wide and slurred S in I, V5, and V6.
 - (b) Terminal, slurred R' in aVR and the RPLs (i.e., V4R, V1, and V2), with an rsR' pattern.
 - (4) ST segment shift and T wave inversion are common in adults but not in children.
 - (5) It is unsafe to make a diagnosis of ventricular hypertrophy in the presence of RBBB, because a greater manifest potential for both ventricles is expected to occur without actual ventricular hypertrophy as a result of asynchronous unopposed forces of the RV and LV (as explained earlier).

**FIGURE 2-17**

Tracing from a 6-year-old boy who had corrective surgery for TOF that involved right ventriculotomy for repair of VSD and resection of infundibular narrowing. The QRS axis is only minimally rightward (about +115 degrees), but the terminal (slurred) portion of the QRS is clearly rightward. The QRS duration is prolonged (0.13 sec). The T vector remains normal (+10 degrees). Although there are abnormally large R voltages in V4R, V1, and V2, with abnormal R/S ratios, one cannot make the diagnosis of an additional RVH; it may all be due to RBBB.

2. Intraventricular block. In intraventricular block, the prolongation is throughout the duration of the QRS complex, and does not resemble either RBBB or LBBB (see Fig. 2-16, D). It is associated with metabolic disorders (hyperkalemia), myocardial ischemia (e.g., during or after cardiopulmonary resuscitation), drugs (e.g., quinidine, procainamide, tricyclic antidepressants), and diffuse myocardial diseases (myocardial fibrosis and systemic diseases with myocardial involvement). Conditions seen with the intraventricular block are often more serious than those seen with BBB or WPW preexcitation.
3. Wolff-Parkinson-White (WPW) preexcitation
 - a. In WPW preexcitation, the initial portion of the QRS complex is slurred, with a “delta” wave (see Fig 2-16, C). Figure 2-18 is an example of WPW preexcitation.
 - b. WPW preexcitation results from an anomalous conduction pathway (i.e., bundle of Kent) between the atrium and the ventricle, bypassing the normal delay of conduction in the AV node.
 - c. In the presence of this finding, diagnosis of ventricular hypertrophy cannot be made safely for the same reason as with BBB.
 - d. Patients with WPW preexcitation are prone to attacks of paroxysmal supraventricular tachycardia (SVT). When there is a history of SVT, the diagnosis of WPW syndrome is justified.

**FIGURE 2-18**

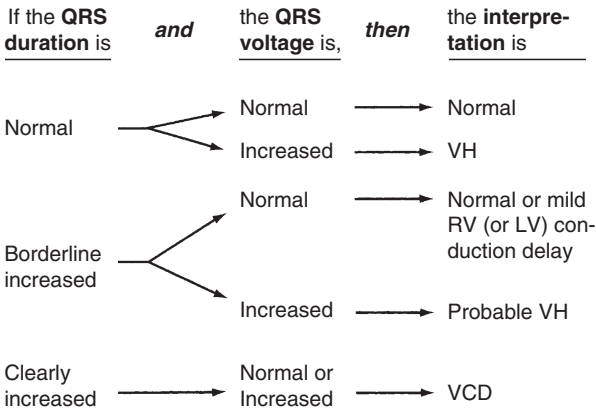
Tracing from a 6-month-old infant with possible glycogen storage disease. The QRS duration is increased to 0.1 seconds (ULN is 0.06 for age). There are delta waves in the initial portion of the QRS complex, which are best seen in I, aVL, and V5. The QRS axis is 0 degree (LAD for age) and the large leftward and posterior QRS voltages are abnormal, but with preexcitation the diagnosis of LVH cannot be made.

e. Criteria for WPW preexcitation

- (1) Short PR interval, less than the lower limits of normal for the patient's age. The lower limits of normal PR interval are as follows:
 - (a) <3 years, 0.08 seconds
 - (b) 3–16 years, 0.1 seconds
 - (c) >16 years, 0.12 seconds
- (2) Delta wave (initial slurring of the QRS complex).
- (3) Wide QRS duration (beyond the ULN).

f. Other rare forms of preexcitation can also result in extreme tachycardia.

- (1) Lown-Ganong-Levine preexcitation is characterized by a short PR interval and normal QRS duration (without a delta wave). James fibers (which connect the atrium and the bundle of His) bypass the upper AV node and produce a short PR interval, but the ventricles are depolarized normally through the His-Purkinje system. When there is history of SVT, the condition may be called Lown-Ganong-Levine syndrome; in the absence of such a history, the ECG should be read as “short PR interval.”
- (2) Mahaim-type preexcitation is characterized by a normal PR interval and long QRS duration with an intermittent delta wave. Mahaim fiber connects the AV node (or lateral right atrial wall) and the right ventricle bypassing the bundle of His and “short-circuiting” into the right ventricle, with resulting QRS complexes of LBBB morphology.

**FIGURE 2-19**

Algorithm for differentiating between ventricular hypertrophy and ventricular conduction disturbances. VCD, ventricular conductive disturbance; VH, ventricular hypertrophy.

4. Ventricular hypertrophy vs. ventricular conduction disturbances

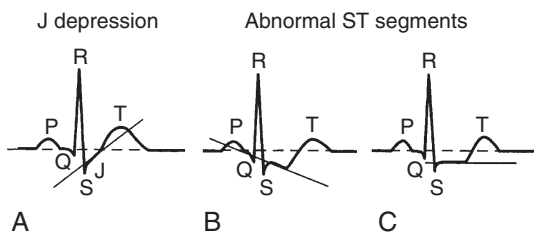
Two common pediatric ECG abnormalities, ventricular hypertrophy and ventricular conduction disturbances, often manifest with increased QRS voltages, and thus are not always easy to differentiate from each other. An accurate measurement of the QRS duration is essential. The following approach may aid in differentiating these two conditions (Fig. 2-19).

- When the QRS duration is normal, normal QRS voltages indicate a normal ECG, and increased QRS voltages may indicate ventricular hypertrophy.
- When the QRS duration is clearly prolonged, normal as well as increased QRS voltages indicate ventricular conduction disturbance. In this situation, an increased QRS voltage does not indicate the presence of an additional ventricular hypertrophy.
- When the QRS duration is only borderline increased, the separation of ventricular hypertrophy and ventricular conduction disturbances is difficult. In general, a borderline increase in the QRS voltage, especially without the terminal or initial slurring, favors ventricular hypertrophy rather than conduction disturbances. When the QRS voltage is normal, the ECG may be interpreted either as normal or as a mild RV or LV conduction delay.

G. Pathologic ST Segment and T Wave Changes

Not all ST segment shifts are abnormal. Elevation or depression of up to 1 mm in the limb leads and up to 2 mm in the precordial leads is within normal limits.

- Nonpathologic ST segment shift.** Two common types of nonpathologic ST segment shifts are J depression and early repolarization. The T vector remains normal in these situations.

**FIGURE 2-20**

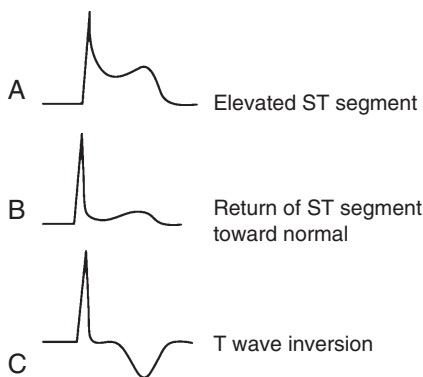
Nonpathologic (nonischemic) and pathologic (ischemic) ST and T changes.

A, Characteristic nonischemic ST segment alteration called J depression; note that the ST slope is upward. **B** and **C**, Ischemic or pathologic ST segment alterations. Downward slope of the ST segment is shown in **B**. Horizontal ST segment is sustained in **C**.

- a. **J depression.** J depression is a shift of the junction between the QRS complex and the ST segment (J point) without sustained ST segment depression (Fig. 2-20, A).
- b. **Early repolarization.** In early repolarization, all leads with upright T waves have elevated ST segments, and leads with inverted T waves have depressed ST segments. This condition, seen in healthy adolescents and young adults, resembles the ST segment shift seen in acute pericarditis; in the former, the ST segment is stable, and in the latter, the ST segment returns to the isoelectric line.
2. **Pathologic ST segment shift.** Abnormal shifts of the ST segment often are accompanied by T wave inversion. A pathologic ST segment shift assumes one of the following forms.
 - Downward slant followed by a diphasic or inverted T wave (see Fig. 2-20, B).
 - Horizontal elevation or depression sustained for >0.08 seconds (see Fig. 2-20, C).

Examples of pathologic ST segment shifts and T wave changes include LVH or RVH with strain; digitalis effects; pericarditis; myocarditis; and myocardial infarction.

- a. **Pericarditis:** The ECG changes seen in pericarditis consist of the following.
 - (1) Pericardial effusion may produce low QRS voltages (with <5 mm in every one of the limb leads).
 - (2) Subepicardial myocardial damage produces the following time-dependent changes in the ST segment and T wave (see Figure 2-21).
 - (a) ST segment elevation in the leads representing the LV.
 - (b) The ST segment shift returning to normal within 2 or 3 days.
 - (c) T wave inversion (with isoelectric ST segment) 2 to 4 weeks after the onset of pericarditis.
- b. **Myocarditis:** ECG findings of rheumatic or viral myocarditis are

**FIGURE 2-21**

Time-dependent changes of the ST segment and T wave in pericarditis. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

relatively nonspecific and may involve all phases of the cardiac cycle: first- or second-degree AV block, low QRS voltages (5 mm or less in all six limb leads), decreased amplitude of the T wave, QT prolongation, and/or cardiac arrhythmias.

- c. **Myocardial infarction (MI):** The ECG findings of myocardial infarction, which are time dependent, are illustrated in [Figure 2-22](#). Leads that show these abnormalities vary with the location of the infarction. They are summarized in [Table 2-9](#).
 - (1) In adult patients with acute MI, the more common ECG findings are those of the early evolving phase, which consists of pathologic Q waves (abnormally wide and deep), ST segment elevation, and T wave inversion.
 - (2) Frequent ECG findings in children with acute MI include wide Q waves, ST segment elevation (>2 mm), and QTc prolongation (>0.44 sec) with accompanying abnormal Q waves.
 - (3) The duration of the pathologic Q wave is ≥ 0.04 seconds in adults; it should be at least 0.03 seconds in children.

H. Electrolyte Disturbances

1. Calcium

- a. **Hypocalcemia** produces the prolongation of the ST segment, with resulting prolongation of the QTc interval. The T wave duration remains normal.
- b. **Hypercalcemia** shortens the ST segment without affecting the T wave, with resultant shortening of the QTc interval ([Fig. 2-23](#)).

2. Potassium

- a. **Hypokalemia** produces one of the least specific ECG changes.
 - (1) When the serum potassium K level is < 2.5 mEq/L, ECG changes

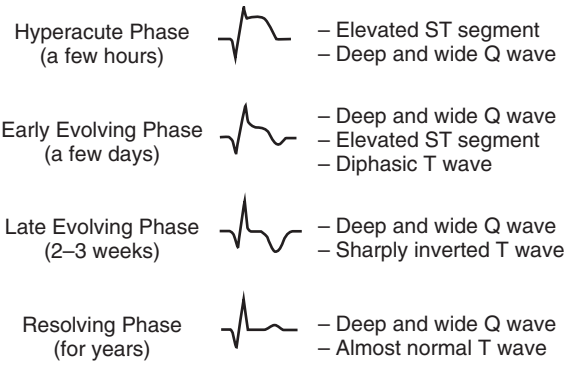


FIGURE 2-22
Sequential changes in the ST segment and T wave in myocardial infarction. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

TABLE 2-9
LEADS SHOWING ABNORMAL ECG FINDINGS IN MYOCARDIAL INFARCTION

	LIMB LEADS	PRECORDIAL LEADS
Lateral	I, aVL	V5, V6
Anterior		V1, V2, V3
Anterolateral	I, aVL	V2 through V6
Diaphragmatic	II, III, aVF	
Posterior		V1 through V3 ^a

^aNone of the leads is oriented toward the posterior surface of the heart. Therefore, ECG changes seen in leads V1 through V3 will be mirror images of expected changes of the infarction (e.g., tall and slightly wide R waves comparable to abnormal Q waves, and tall and wide, symmetric T waves in V1 and V2).

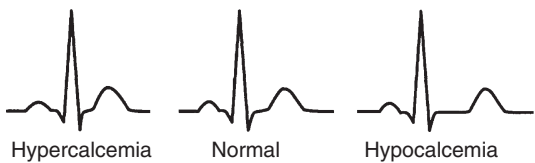
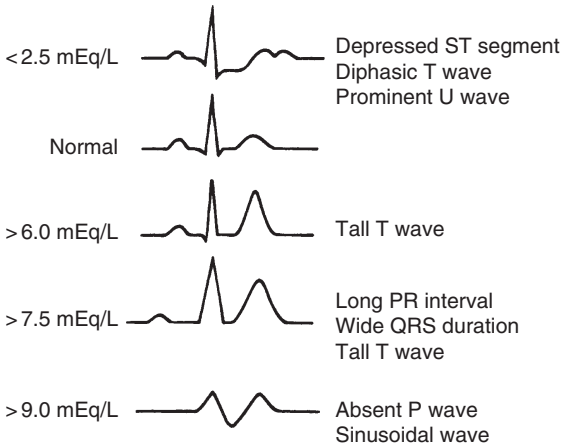


FIGURE 2-23
ECG findings of hypercalcemia and hypocalcemia. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

SERUM K

**FIGURE 2-24**

ECG findings of hypokalemia and hyperkalemia. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

consist of a prominent U wave with apparent prolongation of the QTc interval, flat or diphasic T waves, and ST segment depression (Fig. 2-24).

(2) With further lowering of serum K, the PR interval becomes prolonged, and sinoatrial block may occur.

- b. **Hyperkalemia.** A progressive hyperkalemia produces the following sequential changes in the ECG (Fig. 2-24). These ECG changes are usually seen best in leads II and III and the left precordial leads.

- (1) Tall, tented T waves, best seen in the precordial leads
- (2) Prolongation of QRS duration
- (3) Prolongation of PR interval
- (4) Disappearance of P waves
- (5) Wide, bizarre diphasic QRS complexes (sine wave)
- (6) Eventual asystole

Chapter 3

Chest Roentgenography

3

Chest radiography was an essential part of cardiac evaluation before the echocardiographic (echo) studies became widely available to cardiologists. This simple test remains very useful to physicians who do not have access to the echocardiograph. In addition, cardiovascular abnormalities may be incidentally suspected by chest radiographic films.

Information to be gained from chest radiographs includes (1) heart size and silhouette, (2) enlargement of specific cardiac chambers, (3) pulmonary blood flow (PBF) or pulmonary vascular markings (PVM), and (4) other information regarding lung parenchyma, spine, bony thorax, abdominal situs, and so on.

A. Heart Size and Silhouette

1. Heart size: The cardiothoracic (CT) ratio is obtained by dividing the largest transverse diameter of the heart by the widest internal diameter of the chest (Fig. 3-1). The CT ratio is calculated by the following formula.

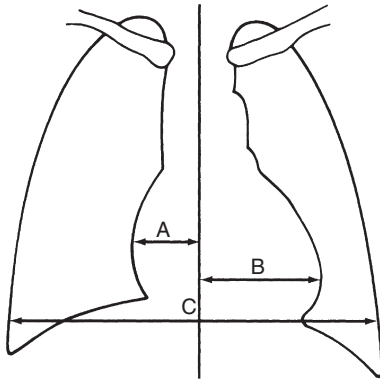
$$\text{CT ratio} = (A + B) \div C$$

A CT ratio of more than 0.5 is considered to indicate cardiomegaly. However, the CT ratio cannot be used with any accuracy in neonates and small infants, in whom a good inspiratory chest film is rarely obtained.

2. Normal cardiac silhouette: The structures that form the cardiac borders in the posteroanterior and lateral projections of a chest radiograph are shown in Figure 3-2. In the neonate, however, a typical normal cardiac silhouette as shown in Figure 3-2 is rarely seen because of the presence of a large thymus.
3. Abnormal cardiac silhouette: The overall shape of the heart sometimes provides important clues to the type of cardiac defect (Fig. 3-3).
 - a. Boot-shaped heart with decreased PVM is seen in infants with cyanotic TOF and in some infants with tricuspid atresia (Fig. 3-3, A).
 - b. Narrow waist and egg-shaped heart with increased PVM in a cyanotic infant strongly suggest TGA (Fig. 3-3, B).
 - c. Snowman sign with increased PVM is seen in infants with the supracardiac type of TAPVR (Fig. 3-3, C).

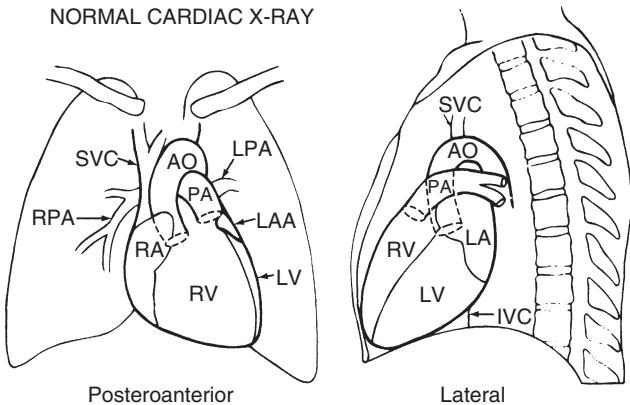
B. Cardiac Chambers and Great Arteries

1. Individual chamber enlargement
 - a. Left atrial enlargement (LAE): Mild LAE is best recognized in the lateral projection by posterior protrusion of the LA border (Fig. 3-4). An enlargement of the LA may produce a double density on the posteroanterior view. With further enlargement, the left atrial appendage

**FIGURE 3-1**

Measurement of the cardiothoracic (CT) ratio from the posteroanterior view of a chest radiograph.

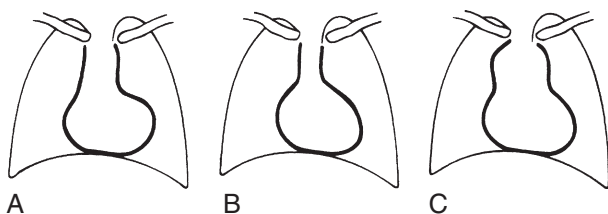
NORMAL CARDIAC X-RAY

**FIGURE 3-2**

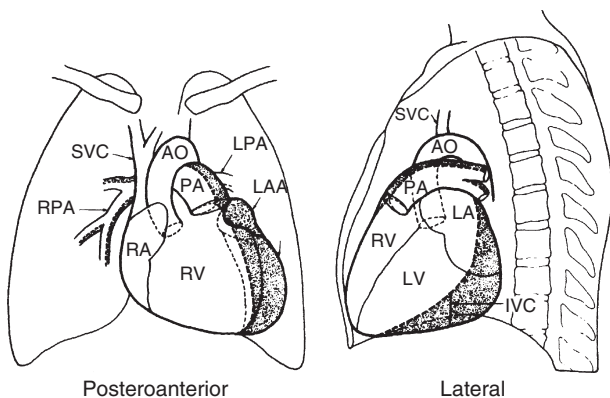
Posteroanterior and lateral projections of normal cardiac silhouette. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

becomes prominent on the left cardiac border, and the left main-stem bronchus is elevated.

- Left ventricular enlargement (LVE): In the posteroanterior view the apex of the heart is displaced to the left and inferiorly. In the lateral view the lower posterior cardiac border is displaced further posteriorly (Fig. 3-4).
- Right atrial enlargement (RAE): In the posteroanterior projection an enlargement of the RA results in an increased prominence of the right lower cardiac border (Fig. 3-5).

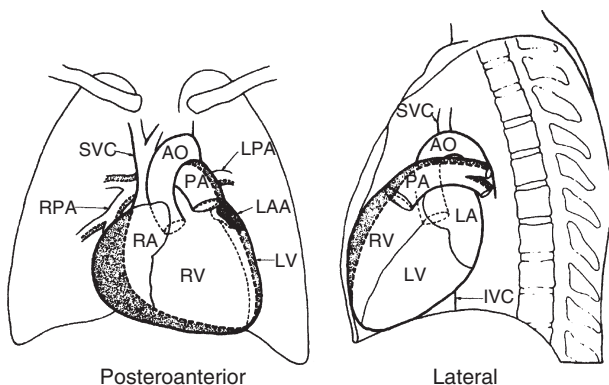
**FIGURE 3-3**

Abnormal cardiac silhouette. **A**, Boot-shaped heart. **B**, Egg-shaped heart. **C**, Snowman sign. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

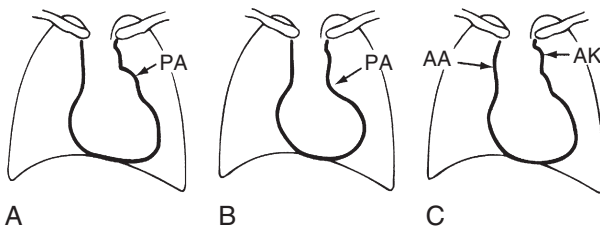
**FIGURE 3-4**

Posteroanterior and lateral view diagrams of CRG demonstrating an enlargement of the LA and LV, as seen in a patient with a moderate VSD. The enlargement of the LA, LV, and main PA and increased pulmonary vascular markings are present.

- d. Right ventricular enlargement (RVE): RVE is best recognized in the lateral view by the filling of the retrosternal space (Fig. 3-5).
2. The size of the great arteries
 - a. Prominent main pulmonary artery (MPA) segment in the posteroanterior view is due to one of the following (Fig. 3-6, A):
 - (1) Poststenotic dilatation (e.g., pulmonary valve stenosis)
 - (2) Increased blood flow through the PA (e.g., ASD, VSD)
 - (3) Increased pressure in the PA (i.e., pulmonary hypertension)
 - (4) Occasional normal adolescence, especially in girls
 - b. A concave MPA segment with resulting boot-shaped heart is seen in TOF and tricuspid atresia (Fig. 3-6, B).

**FIGURE 3-5**

Posteroanterior and lateral view diagrams of CRG demonstrating an enlargement of the RA and RV, as seen in a patient with a large ASD. The pulmonary vascular markings are also increased. The RV enlargement is best seen in the lateral view. AO, aorta; LAA, left atrial appendage. Other abbreviations are found on pages xi to xii.

**FIGURE 3-6**

Abnormalities of the great arteries. **A**, Prominent main PA segment. **B**, Concave PA segment. **C**, Dilation of the ascending aorta (AA) and prominence of the aortic knob (AK). (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- c. Dilatation of the aorta. An enlarged ascending aorta (AA) is seen in AS (due to poststenotic dilatation) and TOF and less often in PDA, COA, or systemic hypertension. When the ascending aorta and aortic arch are enlarged, the aortic knob (AK) may become prominent on the posteroanterior view (Fig. 3-6, C).

C. Pulmonary Vascular Markings

One of the major goals of radiologic examination is the assessment of pulmonary blood flow.

1. Increased pulmonary vascular marking (PVM) is present when the pulmonary arteries appear enlarged and extend into the lateral third of the

lung field, where they are not usually present, and there is an increased vascularity to the lung apices where the vessels are normally collapsed.

- a. Increased PVM in an acyanotic child suggests a left-to-right shunt lesion such as ASD, VSD, PDA, ECD, PAPVR, or any combination of these.
 - b. In a cyanotic infant, an increased PVM may indicate TGA, TAPVR, HLHS, persistent truncus arteriosus, or single ventricle.
2. A decreased PVM is suspected when the hilum appears small, the remaining lung fields appear black, and the vessels appear small and thin. Ischemic lung fields in cyanotic patients suggest critical stenosis or atresia of the pulmonary or tricuspid valves or TOF.
 3. Pulmonary venous congestion, which is characterized by a hazy and indistinct margin of the pulmonary vasculature, is seen with HLHS, MS, TAPVR, cor triatriatum, and so on.
 4. Normal pulmonary vasculature is present in patients with mild to moderate PS and in patients with small L-R shunt lesions.

D. Systematic Approach

The interpretation of chest radiographs should include a systematic routine to avoid overlooking important anatomic changes relevant to cardiac diagnosis.

1. Location of the liver and stomach gas bubble
 - a. The cardiac apex should be on the same side as the stomach or opposite the hepatic shadow.
 - b. When there is heterotaxia, with the apex on the right and the stomach on the left, or vice versa, the likelihood of a serious heart defect is great.
 - c. A midline liver is associated with asplenia (Ivemark's) syndrome or polysplenia syndrome.
2. Skeletal aspect of chest radiographs
 - a. Pectus excavatum may create the false impression of cardiomegaly in the posteroanterior projection.
 - b. Thoracic scoliosis and vertebral abnormalities are frequent findings in cardiac patients.
 - c. Rib notching is a specific finding of COA in a child usually older than 5 years, generally seen between the fourth and eighth ribs.
3. Identification of the aorta
 - a. When the descending aorta is seen on the left of the vertebral column, a left aortic arch is present.
 - b. When the descending aorta is seen on the right of the vertebral column, a right arch is present. A right aortic arch is frequently associated with TOF or persistent truncus arteriosus.
 - c. A "figure 3" in a heavily exposed film or an E-shaped indentation in a barium esophagogram is seen with COA.
4. Upper mediastinum
 - a. The thymus is prominent in healthy infants and may give a false impression of cardiomegaly.
 - b. A narrow mediastinal shadow is seen in TGA or DiGeorge syndrome.

- c. A “snowman” sign is seen in infants (usually older than 4 months) with supracardiac TAPVR.
- 5. Pulmonary parenchyma
 - a. A long-standing density, particularly in the right lower lung field, suggests bronchopulmonary sequestration.
 - b. A vertical vascular shadow along the right lower cardiac border may suggest PAPVR from the lower lobe (the scimitar syndrome).

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SPECIAL TOOLS USED IN CARDIAC EVALUATION

A number of special tools are available to the cardiologist in the evaluation of cardiac patients. Noncardiologists have the opportunity to be exposed to some noninvasive tools, such as echocardiography, exercise stress test, and ambulatory ECG (e.g., Holter monitor). Magnetic resonance imaging (MRI) and computed tomography (CT) are other noninvasive tools that have become popular in recent years. Cardiac catheterization and angiocardiology are invasive tests. Although catheter intervention procedures are not diagnostic, they are included in this section because they are usually performed with cardiac catheterization.

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Noninvasive Imaging Tools

I. ECHOCARDIOGRAPHY

Echocardiography (echo) is an extremely useful noninvasive test used in the diagnosis and management of heart disease. An echo study currently begins with real-time two-dimensional echo, which produces high-resolution tomographic images of cardiac structures and their movement, and vascular structures leaving and entering the heart. With the support of Doppler and color flow mapping, echo studies provide reliable anatomic and quantitative information such as ventricular function, pressure gradients across cardiac valves and blood vessels, and estimation of pressures in the great arteries and ventricles.

A. Two-Dimensional Echocardiography

Routine two-dimensional echocardiography (2D echo) is obtained from four transducer locations: parasternal, apical, subcostal, and suprasternal notch positions. Abdominal and subclavicular views are also useful.

Figures 4-1 through 4-9 illustrate selected standard 2D echo images of the heart and great vessels. A brief description of the standard 2D echo views follows.

Selected normal dimensions of cardiac structures and the great arteries are presented in Appendix D. These tables are frequently used in practice of pediatric cardiology. They include M-mode measurements of the LV (Table D-1); stand-alone M-mode measurements of the RV, aorta, and LA (Table D-2); aortic root and aorta (Table D-3); pulmonary valve and pulmonary arteries (Table D-4); and atrioventricular valves (Table D-5). Normal dimensions of coronary arteries are shown in Table D-6.

1. Parasternal Long-Axis Views (Fig. 4-1)

- a. The standard long-axis view (Fig. 4-1, A).
 - (1) This is a very important view in evaluating abnormalities in or near the mitral valve, LA, LV, LVOT, aortic valve, aortic root, ascending aorta, and ventricular septum.
 - (2) In the normal heart there is aortic-mitral continuity (i.e., the anterior mitral leaflet is contiguous with the posterior wall of the aorta).
 - (3) The right and noncoronary cusps of the aortic valve are imaged but the left coronary sinus cusp is out of this plane.
 - (4) VSDs of tetralogy of Fallot (TOF) and persistent truncus arteriosus are readily seen adjacent to the aortic valve.
 - (5) The anterior and posterior leaflets of the mitral valve and their chordal and papillary muscle attachments are imaged. Mitral valve prolapse (MVP) is best evaluated in this view.

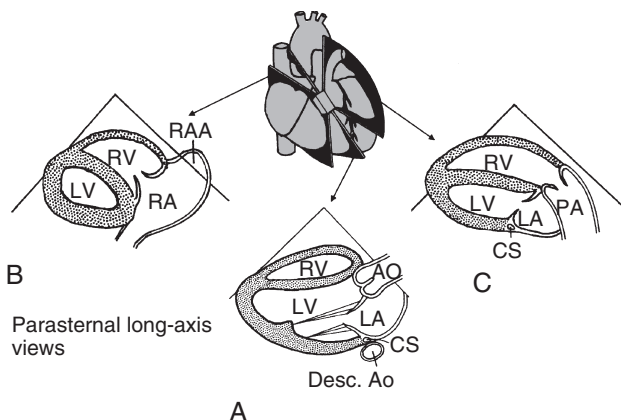
**FIGURE 4-1**

Diagram of important two-dimensional echo views obtained from the parasternal long-axis transducer position. **A**, Standard long-axis view, **B**, RV inflow view, and **C**, RV outflow view. AO, aorta; CS, coronary sinus; Desc. Ao, descending aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RAA, right atrial appendage; RV, right ventricle. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- (6) The coronary sinus is seen frequently as a small circle in the atrioventricular groove. An enlarged coronary sinus (CS) may suggest left SVC, TAPVR to coronary sinus, coronary AV fistula, and rarely elevated RA pressure.
- (7) Pericardial effusion is readily seen in this view.
- b. The RV inflow view (Fig. 4-1, B).
 - (1) This view shows abnormalities of the RA cavity, RV inflow, and the tricuspid valve.
 - (2) Abnormalities in the tricuspid valve (regurgitation, prolapse) are evaluated. It is a good view to record the velocity of the TR jet (to estimate RV systolic pressure).
 - (3) The ventricular septum near the TV is the inlet muscular septum; the remainder is the trabecular septum.
 - (4) The right atrial appendage (RAA) can also be imaged in this view.
- c. The RV outflow view (Fig. 4-1, C).
 - (1) Abnormalities in the RVOT, pulmonary valve, and main PA are readily imaged and their severity easily estimated.
 - (2) The supracristal infundibular (outlet) septum is seen near the pulmonary valve.
2. Parasternal Short-Axis Views: These views evaluate the aortic valve, coronary arteries, mitral valve, and papillary muscles.
 - a. The aortic valve level (Fig. 4-2, A).

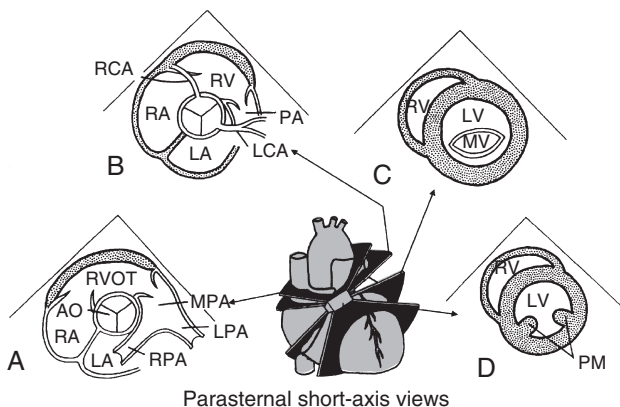
**FIGURE 4-2**

Diagram of a family of parasternal short-axis views. **A**, Semilunar valves and great arteries level. **B**, Coronary artery level. **C**, Mitral valve level. **D**, Papillary muscle level. AO, aorta; LA, left atrium; LCA, left coronary artery; LPA, left pulmonary artery; LV, left ventricle; MPA, main pulmonary artery; MV, mitral valve; PM, papillary muscle; RA, right atrium; RCA, right coronary artery; RPA, right pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- (1) The normal aortic valve has a circle with a tri-leaflet aortic valve that has the appearance of the letter “Y” during diastole. Abnormalities of the aortic valve (bicuspid, unicuspid, or dysplastic) are evaluated in this view.
 - (2) Stenoses of the pulmonary valve and PA branches can be evaluated by Doppler and color flow mapping.
 - (3) PDA is interrogated with color flow imaging and Doppler study.
 - (4) The membranous VSD is seen just distal to the tricuspid valve (at the 10 o'clock position).
 - (5) Both the infracristal and supracristal outlet VSDs are imaged anterior to the aortic valve near the pulmonary valve (at the 12 to 2 o'clock position).
- b. Coronary arteries (Fig. 4-2, B).
- (1) The right CA arises from the anterior coronary cusp.
 - (2) The left main CA arises in the left coronary cusp near the main pulmonary artery. Its bifurcation into the left anterior descending and circumflex coronary artery is usually imaged.
 - (3) The dimension of the coronary arteries is measured in this view (see Table D-6 in Appendix D).
- c. The mitral valve. The mitral valve is seen as a “fish mouth” during diastole (Fig. 4-2, C).

d. Papillary muscles (Fig. 4-2, D).

(1) Two papillary muscles are normally seen at the 4 o'clock (antero-lateral) and 8 o'clock (posteromedial) positions. Occasionally, accessory papillary muscles or left ventricular strands are imaged in the normal heart.

(2) The ventricular septum seen at this level is the trabecular septum.

3. Apical Four-Chamber Views (Fig. 4-3)

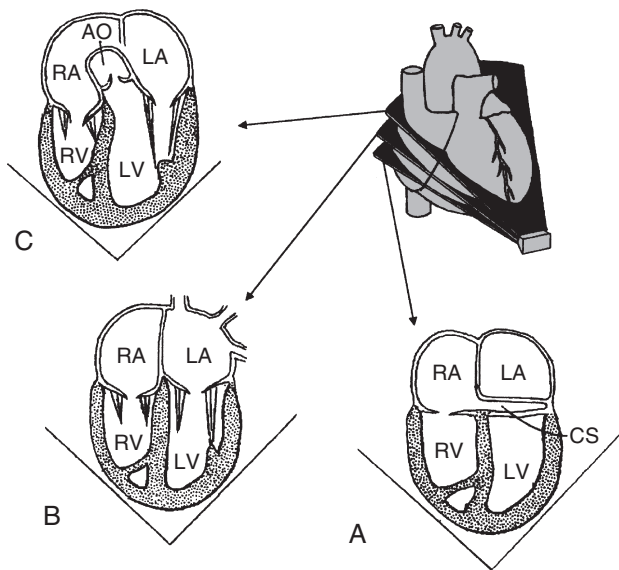
a. The coronary sinus (Fig. 4-3, A) is seen in the most posterior plane. The ventricular septum seen in this view is the posterior trabecular septum.

b. The middle plane of the apical four-chamber view (Fig. 4-3, B).

(1) This view is good to evaluate the atrial and ventricular chambers, such as relative size and contractility of atrial and ventricular chambers, AV valve abnormalities, and images of some pulmonary veins.

(2) The relative position of the tricuspid valve helps to identify the anatomic right and left ventricles.

(a) Normally the tricuspid valve (TV) insertion to the septum is more apicalward than the mitral valve (5-10 mm in older children



Apical four-chamber views

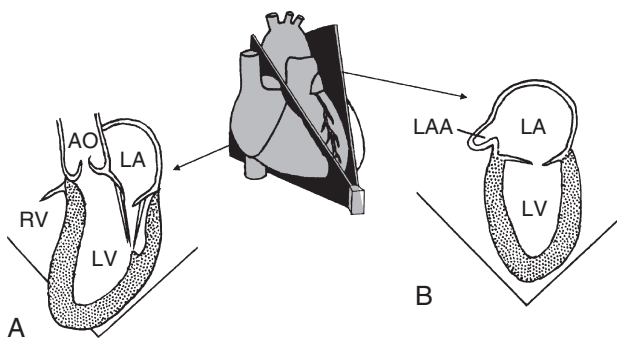
FIGURE 4-3

Diagram of two-dimensional echo views obtained with the transducer at the apical position. **A**, The posterior plane view. **B**, The standard apical four-chamber view. **C**, The apical "five-chamber" view. AO, aorta; CS, coronary sinus; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

and adults). The ventricle attached to the TV is the RV. (The TV insertion is displaced more apically in Ebstein anomaly.)

(b) The anatomic RV is also heavily trabeculated and has the moderator band. (The left ventricle is smooth walled without prominent muscle bundles.)

- The inlet ventricular septum (where an ECD occurs) is imaged just under the AV valves; the remainder of the septum is the trabecular septum. (The membranous septum is *not* imaged in this view.)
 - The presence and severity of regurgitation of both AV valves are evaluated in this view.
 - The inflow velocities of both the mitral and tricuspid valves are measured here.
 - The TR jet velocity is measured (to estimate RV systolic pressure).
 - Abnormal chordal attachment of the atrioventricular valve (straddling) and overriding of the septum are also noted in this view.
 - Pericardial effusion is easily detected in this view.
- c. The apical “five-chamber” view (Fig. 4-3, C) is obtained by further anterior angulation of the transducer.
- (1) The LVOT, aortic valve, subaortic area, and proximal ascending aorta are shown in this view.
 - (2) Stenosis and regurgitation of the aortic valve and the anatomy of the LV outflow tract (including subaortic membrane) are best evaluated in this view.
 - (3) The membranous VSD is visualized just under the aortic valve.
4. Apical Long-Axis Views (Fig. 4-4, A)
- a. The apical long-axis view (or apical three-chamber view) shows structures similar to those seen in the parasternal long-axis view.



Apical long-axis views

FIGURE 4-4

Apical long-axis views. **A**, Apical “three-chamber” view. **B**, Apical “two-chamber” view. AO, aorta; LA, left atrium; LAA, left atrial appendage; LV, left ventricle; RV, right ventricle. (From Park MK: *Park’s Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- b. The apical two-chamber view (Fig. 4-4, B).
 - (1) The LA, mitral valve, and LV are imaged. The left atrial appendage (LAA) can also be imaged.
 - (2) The view of the LV apex provides diagnostic clues for cardiomyopathy, apical thrombus, and aneurysm.
5. Subcostal Long-Axis (Coronal) Views (Fig. 4-5): These views are shown from posterior to anterior direction.
 - a. The coronary sinus is seen posteriorly (Fig 4-5, A). This plane shows structures similar to those shown in Figure 4-3, A.
 - b. The standard subcostal four-chamber view (Fig. 4-5, B) is obtained by anterior angulation. This view emphasizes the atrial septum and its morphologic features, including the atrial septal defect and atrial septal aneurysm.
 - c. Further anterior angulation (Fig. 4-5, C).
 - (1) The LV outflow tract, aortic valve, and ascending aorta are imaged.
 - (2) Four parts of the ventricular septum can be imaged from this transducer position: trabecular (in A); inlet (in B); membranous (in C), and subaortic outlet (in D).

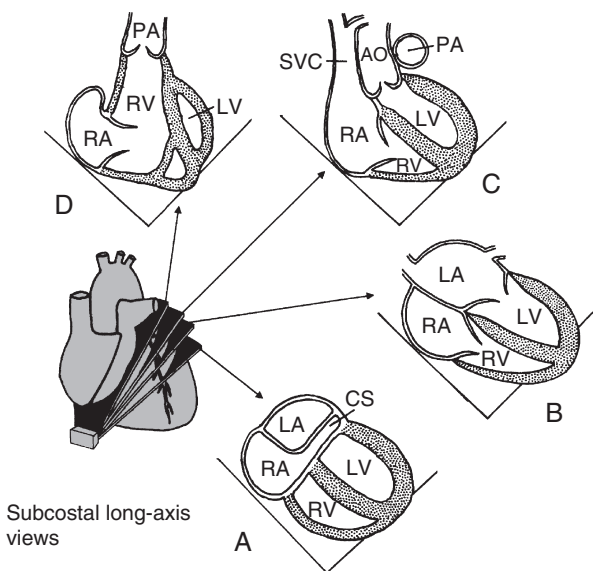
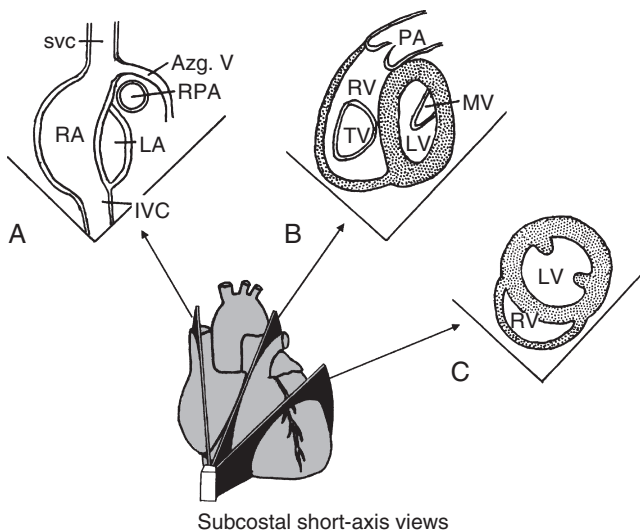
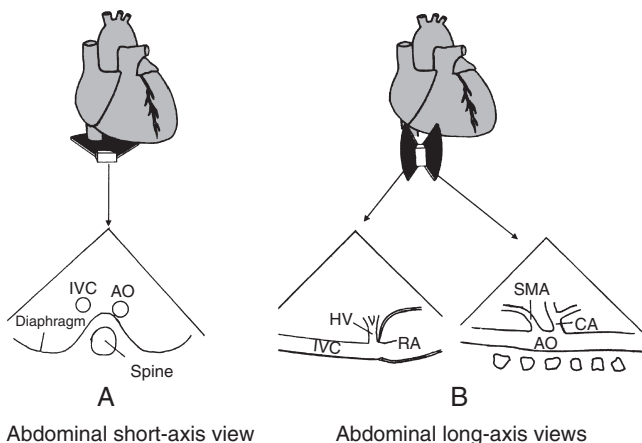
**FIGURE 4-5**

Diagram of subcostal long-axis views. **A**, Coronary sinus view posteriorly. **B**, Standard subcostal four-chamber view. **C**, View showing the LV outflow tract and the proximal aorta. **D**, View showing the RV outflow tract and the proximal main pulmonary artery. AO, aorta; CS, coronary sinus; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; SVC, superior vena cava. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- (3) The junction of the superior vena cava and the RA is seen to the right of the ascending aorta.
- d. Further anterior angulation (Fig. 4-5, D) shows the entire RV (including the inlet, trabecular, and infundibular portions), the pulmonary valve, and the main pulmonary artery. Stenosis of the pulmonary valve and the anatomy of the RV outflow tract can be evaluated in this view.
6. Subcostal Short-Axis (or Sagittal) Views (Fig. 4-6)
- a. Figure 4-6, A:
- (1) Both the SVC and IVC are seen to connect to the RA.
 - (2) A small azygos vein and the right PA can also be seen in this view.
 - (3) In patients with ASD, the size of the posterosuperior (PS) and postero-inferior (PI) rims of atrial septal defect are measured in this view.
- b. A leftward angulation (Fig. 4-6, B) shows the RV outflow tract, pulmonary valve, and pulmonary artery. The tricuspid valve is seen on end.
- c. Further leftward angulation (Fig. 4-6, C) shows views similar to the parasternal short-axis view (Fig 4-2, D).
7. Subcostal Views of the Abdomen
- a. Abdominal short-axis view (left panel of Fig. 4-7).

**FIGURE 4-6**

Subcostal short-axis (sagittal) views. **A**, Entry of venae cavae with drainage of the azygos vein. **B**, View showing the RV, RV outflow tract, and pulmonary artery. **C**, Short-axis view of the ventricles. Azg. V, azygos vein; LA, left atrium; LV, left ventricle; MV, mitral valve; PA, pulmonary artery; RA, right atrium; RPA, right pulmonary vein; RV, right ventricle; SVC, superior vena cava; TV, tricuspid valve. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

**FIGURE 4-7**

Subcostal abdominal views. **Left**, abdominal short-axis view. **Right**, abdominal long-axis view. **A**, IVC view; **B**, Abdominal descending aorta view. AO, aorta; CA, celiac axis; HV, hepatic vein; IVC, inferior vena cava; RA, right atrium; SMA, superior mesenteric artery. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- (1) This view shows the descending aorta on the left and the inferior vena cava (IVC) on the right of the spine. The aorta should pulsate.
 - (2) Both hemidiaphragms are seen, which move symmetrically with respiration. (Asymmetric or paradoxical movement of the diaphragm is seen with paralysis of the hemidiaphragm).
- b. Abdominal long-axis views (right panel of Fig. 4-7).
- (1) Right panel of Figure 4-7, A
 - (a) The IVC is imaged longitudinally to the right of the spine.
 - (b) The IVC collects the hepatic vein (HV) before draining into the RA. The failure of the IVC to join the RA indicates interruption of the IVC (with azygous continuation), which is seen in polysplenia syndrome.
 - (c) The Eustachian valve may be seen at the junction of the IVC and the RA.
 - (2) Right panel of Figure 4-7, B
 - (a) The descending aorta is imaged longitudinally to the left of the spine.
 - (b) The celiac artery (CA) and the superior mesenteric artery (SMA) are easily imaged.
 - (c) A pulsed wave Doppler examination of the abdominal aorta in this view is helpful in identifying the coarctation by demonstrating delayed rate of systolic upstroke and persistent diastolic flow.

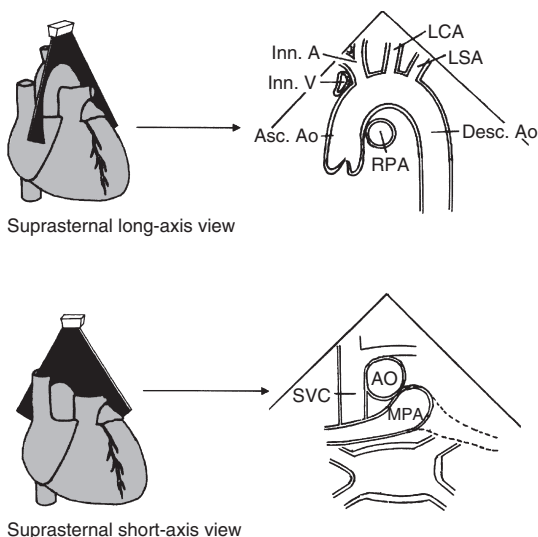
**FIGURE 4-8**

Diagram of suprasternal notch two-dimensional echo views. **Upper panel:** Long-axis view. **Lower panel:** Short-axis view. AO, aorta; Asc. Ao, ascending aorta; Desc. Ao, descending aorta; Inn. A, innominate artery; Inn. V, innominate vein; LA, left atrium; LCA, left carotid artery; LSA, left subclavian artery; MPA, main pulmonary artery; PA, pulmonary artery; RPA, right pulmonary artery; SVC, superior vena cava. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

8. Suprasternal Long-Axis View (upper panel of Fig. 4-8)
 - a. This view images the entire (left) aortic arch. Failure to visualize the aortic arch in the usual manner may suggest the presence of a right aortic arch.
 - b. Three arteries arising from the aortic arch are the innominate (or brachiocephalic), left carotid, and left subclavian arteries.
 - c. The innominate vein is seen in front of and the right PA is seen behind the ascending aorta.
 - d. Good images of the isthmus and upper descending aorta are very important to diagnose coarctation of the aorta.
 - e. Doppler studies with the cursor placed proximal and distal to the coarctation are important in estimating the severity of the narrowing.
9. Suprasternal Short-Axis View (lower panel of Fig. 4-8)
 - a. The superior vena cava (SVC) is seen to the right of the circular transverse aorta. The innominate vein is seen superior to the circular aorta.

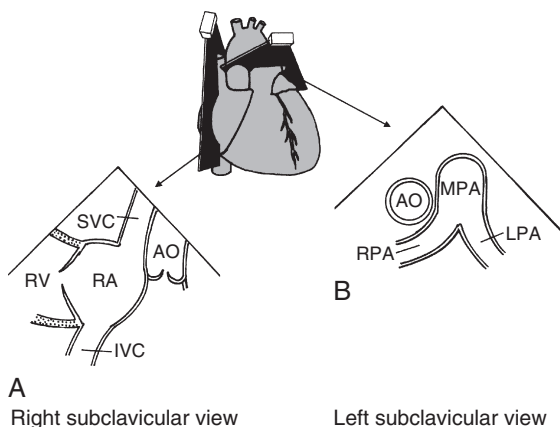
**FIGURE 4-9**

Diagram of subclavicular views. **A**, Right subclavicular view. **B**, Left subclavicular view. AO, aorta; IVC, inferior vena cava; LPA, left pulmonary artery; MPA, main pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RV, right ventricle; SVC, superior vena cava. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- b. The right PA is seen in its length under the circular aorta.
- c. The left innominate vein can be imaged, which arises from the SVC and traverses superior to the circular aorta.
- d. Beneath the right PA is the left atrium (LA). Four pulmonary veins are imaged with a slight posterior angulation.

10. The Subclavicular Views

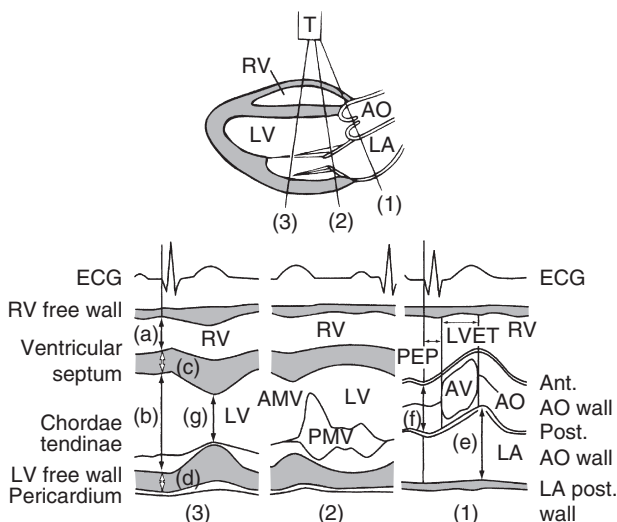
- a. The right subclavicular view (Fig. 4-9, A). This view is useful in the assessment of the SVC and the RA junction as well as the ascending aorta.
- b. The left subclavicular view (Fig. 4-9, B). This view is useful for examination of the branch pulmonary arteries.

B. M-Mode Echocardiography

The M-mode echo provides an “ice-pick” view of the heart. It has limited capability in demonstrating the spatial relationship of structures but remains an important tool in the evaluation of certain cardiac conditions and functions, particularly by measurements of dimensions and timing. It is usually performed as part of 2D echo studies.

1. M-Mode Echo Recording (Fig. 4-10)

- a. Line 1 passes through the aorta (AO) and left atrium (LA), where the dimensions of these structures are measured.

**FIGURE 4-10**

Examples of M-mode recording and measurement of cardiac dimensions. The dimension of the aorta (AO) and left atrium (LA) is measured along line (1). Line (2) passes through the mitral valve and records the movement of the anterior and posterior mitral leaflets. Measurement of chamber dimensions and wall thickness of right and left ventricles is made along line (3). The following measurements are shown in this figure: (a), right ventricular (RV) dimension; (b), left ventricular (LV) diastolic dimension; (c), interventricular septal thickness; (d), LV posterior wall thickness; (e), LA dimension; (f), aortic dimension; (g), LV systolic dimension. AMV, anterior mitral valve; ECG, electrocardiogram; PMV, posterior mitral valve; T, transducer. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- b. Line 2 traverses the mitral valve. Anterior and posterior mitral valve motion is recorded for analysis.
- c. Line 3 goes through the main body of the RV and LV. Along line 3, the dimensions of the RV and LV and the thickness of the interventricular septum and LV posterior wall are measured during systole and diastole. Pericardial effusion is best detected on line 3.
2. **Cardiac Chamber Dimensions.** Most dimensions are measured during diastole, coincident with the onset of the QRS complex; the LA dimension and LV systolic dimension are exceptions (see Fig. 4-10). Normal values are shown as a function of growth (see Appendix D).
3. **Left Ventricular Systolic Function.** LV systolic function is evaluated by the fractional shortening (or shortening fraction) or ejection fraction.

- a. **Fractional shortening** (or shortening fraction) is derived by the following formula:

$$FS (\%) = Dd - Ds / Dd \times 100$$

where FS is fractional shortening, Dd is end-diastolic dimension of the LV, and Ds is end-systolic dimension of the LV. This is a reliable and reproducible index of LV function, provided there is no regional wall-motion abnormality and there is concentric contractility of the LV.

- (1) Mean normal value of FS is 36%, with 95% prediction limits of 28% to 44%.
 - (2) Fractional shortening is decreased in a poorly compensated LV regardless of cause (e.g., pressure overload, volume overload, primary myocardial disorders, and doxorubicin cardiotoxicity).
 - (3) FS is increased in some volume-overloaded ventricle (e.g., VSD, PDA, AR, and MR) and hypertrophic cardiomyopathy (HCM).
 - (4) If the interventricular septal motion is flat or paradoxical, the shortening fraction will not accurately reflect ventricular ejection.
- b. **Ejection fraction** relates to the change in volume of the LV with cardiac contraction. It is obtained by the following formula:

$$EF (\%) = (Dd)^3 - (Ds)^3 / (Dd)^3 \times 100$$

where EF is the ejection fraction and Dd and Ds are end-diastolic and end-systolic dimensions, respectively, of the LV.

- (1) Normal mean ejection fraction is 66% with ranges of 56% to 78%.
- (2) The ejection fraction is a derivative of the fractional shortening and offers no advantages over the fractional shortening. In the above formula, the minor axis is assumed to be half of the major axis of the LV; this assumption is incorrect in children.

C. Color Flow Mapping

A color-coded Doppler provides images of the direction and disturbances of blood flow superimposed on the echo structural image. In general, red is used to indicate flow toward the transducer and blue is used to indicate flow away from the transducer. A turbulent flow appears as light green. This is useful in the detection of shunt or valvular lesions. Color may not appear when the direction of flow is perpendicular to the ultrasound beam.

D. Doppler Echocardiography

A Doppler echo combines the study of cardiac structure and blood flow profiles. Doppler ultrasound equipment detects frequency shifts and thus determines the direction and velocity of blood flow with respect to the ultrasound beam. By convention, velocities of red blood cells moving toward the transducer are displayed above a zero baseline; those moving away from the transducer are displayed below the baseline. The Doppler

TABLE 4-1

NORMAL DOPPLER VELOCITIES IN CHILDREN AND ADULTS: MEAN (RANGES) (M/SEC)

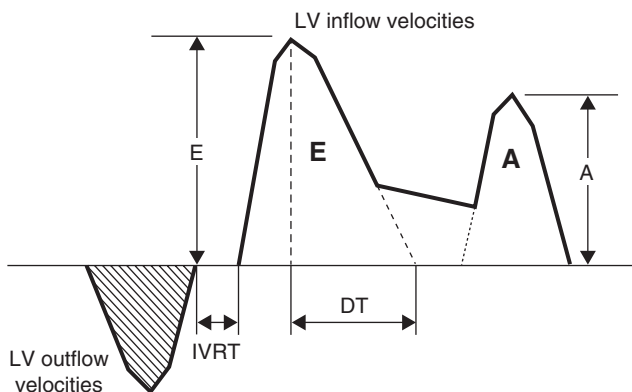
	CHILDREN	ADULTS
Mitral flow	1.0 (0.8-1.3)	0.9 (0.6-1.3)
Tricuspid flow	0.6 (0.5-0.8)	0.6 (0.3-0.7)
Pulmonary artery	0.9 (0.7-1.1)	0.75 (0.6-0.9)
Left ventricle	1.0 (0.7-1.2)	0.9 (0.7-1.1)
Aorta	1.5 (1.2-1.8)	1.35 (1.0-1.7)

From Hatle L, Angelsen B: Doppler Ultrasound in Cardiology, ed 2, Philadelphia, Lea & Febiger, 1985.

4

echo is usually used with color flow mapping to enhance the technique's usefulness.

- The two commonly used Doppler techniques are continuous wave and pulsed wave.
 - The pulsed wave (PW) emits a short burst of ultrasound, and the Doppler echo receiver "listens" for returning information. The PW Doppler can control the site at which the Doppler signals are sampled, but the maximal detectable velocity is limited, making it unusable for quantification of severe obstruction.
 - The continuous wave (CW) emits a constant ultrasound beam with one crystal, and another crystal continuously receives returning information. The CW Doppler can measure extremely high velocities (e.g., for the estimation of severe stenosis), but it cannot localize the site of the sampling; rather, it picks up the signal anywhere along the Doppler beam.
 - When these two techniques are used in combination, clinical application expands.
- Normal Doppler velocities in children and adults are shown in [Table 4-1](#).
 - Normal Doppler velocity is less than 1 m/sec for the pulmonary valve but it may be up to 1.8 m/sec for the ascending and descending aortas.
 - Doppler studies from the atrioventricular valves. Doppler tracings from the mitral and tricuspid valves provide some indices of ventricular diastolic function. They are obtained from the apical four-chamber view with the Doppler sample volume placed in the valve orifices.
 - Normally, the E wave is taller than the A wave ([Fig. 4-11](#)), except for the first 3 weeks of life, during which the A wave may be taller than the E wave.
 - Normal mitral Doppler indices (for children and young adults) are as follows (mean \pm SD). The average peak E velocity is 0.73 ± 0.09 m/sec, the average peak A velocity is 0.38 ± 0.089 m/sec, and the average E:A velocity ratio is 2.0 ± 0.5 .
 - With stenosis of the atrioventricular valves, the flow velocities of the E and A waves increase.

**FIGURE 4-11**

Selected parameters of diastolic function (see text for discussion). A, A wave; DT, deceleration time; E, E wave; IVRT, isovolumic relaxation time; LV, left ventricle.

(Modified from Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

3. Measurement of Pressure Gradients

- a. The simplified Bernoulli equation is used to estimate the pressure gradient across a stenotic lesion, regurgitant lesion, or shunt lesion. One of the following equations may be used.

$$P_1 - P_2 \text{ (mm Hg)} = 4(V_2^2 - V_1^2)$$

$$P_1 - P_2 \text{ (mm Hg)} = 4(V_{\text{max}})^2$$

where $(P_1 - P_2)$ is the pressure difference across an obstruction, V_1 is the velocity (m/sec) proximal to the obstruction, and V_2 is the velocity (m/sec) distal to the obstruction in the first equation. When V_1 is less than 1 m/sec, it can be ignored, as in the second equation. However, when V_1 is more than 1.5 m/sec, it should be incorporated in the equation to obtain a more accurate estimation of pressure gradients. This is important in the study of the ascending and descending aortas (for possible coarctation) where flow velocities are often more than 1.5 m/sec. Ignoring V_1 may significantly overestimate pressure gradient in patients with aortic stenosis or coarctation of the aorta.

- b. The pressure gradient calculated from the Bernoulli equation is the peak instantaneous pressure gradient, *not* the peak-to-peak pressure gradient measured during cardiac catheterization. The peak instantaneous pressure gradient is generally larger than the peak-to-peak pressure gradient. The difference between the two is more noticeable in patients with mild to moderate obstruction and less apparent in patients with severe obstruction.

4. **Estimation of Intracardiac or Intravascular Pressures.** The Doppler echo allows estimation of pressures in the RV, PA, and LV using the flow velocity of valvular or shunt jets. The following are some examples of such applications.

- a. RV (or PA) systolic pressure (SP) can be estimated from the velocity of the tricuspid regurgitation (TR) jet, if present, by the following equation:

$$\text{RVSP (or PASP)} = 4(V)^2 + \text{RA pressure}$$

where V is the TR jet velocity. For example, if the TR velocity is 2.0 m/sec, the instantaneous pressure gradient is $4 \times (2.0)^2 = 4 \times 4.0 = 16$ mm Hg. Using an assumed RA pressure of 10 mm Hg, the RV systolic pressure (or PA systolic pressure in the absence of pulmonary stenosis) is 26 mm Hg. The upper limit of normal Doppler-estimated PA systolic pressure is about 37 mmHg.

- b. RV (or PA) systolic pressure can also be estimated from the velocity of the VSD jet by the following equation:

$$\text{RVSP (or PASP)} = \text{Systemic SP (or arm SP)} - 4(V)^2$$

where V is the VSD jet. For example, if the VSD jet flow velocity is 3 m/sec, the instantaneous pressure drop between the LV and RV is $4 \times 3^2 = 36$ mm Hg. That is, the RV systolic pressure is 36 mm Hg lower than the LV systolic pressure. If the arm systolic blood pressure is 90 mm Hg (which is close to but usually higher than the LV systolic pressure), the RV pressure is estimated to be $90 - 36 = 54$ mm Hg. In the absence of PS, the PA systolic pressure will be approximately 54 mm Hg.

5. **Diastolic Function.** Signs of diastolic dysfunction may precede those of systolic dysfunction. As discussed earlier in this chapter, using mitral inflow velocities obtained in the apical four-chamber view, LV diastolic function can be evaluated. LV diastolic dysfunction is easy to find but it is usually nonspecific and does not provide independent diagnostic information. Two well-known patterns of abnormal diastolic function are a decreased relaxation pattern and a “restrictive” pattern (see Figure 11-2).

II. RADIOLOGIC TECHNIQUES

Although the conventional echo study remains the mainstay of noninvasive evaluation of cardiac patients, it has limitations. In addition to being operator dependent, echocardiography may not provide optimal quality of images of cardiovascular (CV) structures due to postoperative scars, chest wall deformities, overlying lung tissue, large body size in adolescents, and obesity. In particular, extracardiac structures such as the pulmonary arteries, pulmonary veins, and aortic arch cannot always be adequately imaged by echo study due to acoustic window limitations. As for the coronary arteries, only the proximal portion can be adequately imaged by echo studies.

A. Advantages and Disadvantages of Techniques

Both magnetic resonance imaging (MRI) and cardiac computed tomography (CT) can provide images of CV structures and other intrathoracic structures that are not usually imaged by echo studies. However, one of the radiologic techniques may be better than the other in its capability and its practicality. Physicians and cardiologists often must decide which noninvasive technique to use to best serve their patients. This section provides some insights into the advantages and disadvantages of MRI and CT (summarized in [Box 4-1](#)).

B. Choice of Imaging Modalities According to Age Groups

- 1. For infants and children younger than 8 years
 - a. Echo studies will provide accurate diagnosis of even complex CHDs in most cases. Therefore, the need for using MRI or CT study arises only rarely.
 - b. MRI can be used to answer most of the unanswered questions regarding ventricular size and function and extracardiac vasculature.
 - c. When the question is primarily about the extracardiac vasculature, CT can also be used. Its use should be balanced against the risk of ionizing radiation exposure.
- 2. For adolescents and adults
 - a. Although echo remains the primary diagnostic modality, MRI plays an increasing role, especially for the evaluation of the extracardiac

BOX 4-1		
ADVANTAGES AND DISADVANTAGES OF MRI AND CT		
	ADVANTAGES	DISADVANTAGES
MRI	No radiation Excellent in assessment of ventricular function (such as LV and RV volume, mass, and function, including regurgitation fraction) Excellent tissue differentiation Lack of dependence on a rapid bolus of IV contrast	Long scanning time (45-60 min) Need for sedation and anesthesia, requiring close monitoring Metallic artifacts Contraindicated in patients with a pacemaker or ICD
CT	Short total scan time (5-10 min) Fewer requirements of sedation Excellent quality images of extracardiac vasculature (such as pulmonary arteries and veins, aortic arch, coronary arteries, and aortic collaterals) Simultaneous evaluation of lungs and airways High spatial resolution	Radiation exposure Risk of iodinated contrast material Requires breath-hold and low, regular heart rate Lack of information on ventricular function (e.g., RV function, pulmonary regurgitation fraction)

ICD, implantable cardioverter-defibrillator; IV, intravenous; LV, left ventricular; RV, right ventricular.

thoracic vasculature, ventricular volume and function, and flow measurement.

- b. MRI is usually preferred over CT or cardiac catheterization in this age group because it avoids exposure to ionizing radiation and can provide a wealth of functional information.
- c. CT is used in patients with contraindications to MRI, such as those with a cardiac pacemaker or ICD, and those in whom concomitant evaluation for coronary disease is necessary.

Chapter 5

Other Noninvasive Tools

5

Besides noninvasive imaging tools, there are other noninvasive investigational tools that are frequently used in the evaluation of cardiac patients. They include exercise stress testing, long-term ECG monitoring, and ambulatory BP monitoring.

I. EXERCISE STRESS TESTING

Exercise stress testing plays an important role in the evaluation of cardiac symptoms by quantifying the severity of the cardiac abnormality and assessing the effectiveness of management. Although some exercise laboratories have developed bicycle ergometer protocols, the treadmill protocols, such as the Bruce protocol, are well standardized and widely used because most hospitals have treadmills.

A. Monitoring During Exercise Stress Testing

During exercise stress testing, the patient is continually monitored for symptoms such as chest pain or faintness, ischemic changes or arrhythmias on the ECG, oxygen saturation, and responses in heart rate and blood pressure.

1. **Endurance time.** There is a high correlation between the maximum oxygen consumption ($\text{Vo}_2 \text{ max}$) and endurance time. Thus endurance time is the best predictor of exercise capacity in children. The endurance data reported by Cummings et al in 1978 have served as the reference for several decades. Two recent reports from the U.S. (Chatrath et al, 2002; Ahmed et al, 2001) indicate that the endurance time has been reduced significantly since the 1970s. It is concerning that endurance times reported from two other countries (Italy in 1994; Turkey in 1998) are similar to those published by Cummings et al and are significantly longer than those reported in the two U.S. reports. This may be an indication that U.S. youth are less physically fit than the youth from other countries, which may lead to increased risk of coronary artery disease and stroke in the U.S. population. A new set of endurance data from a recent U.S. study is presented in [Table 5-1](#).
2. **Heart rate.** Heart rate is measured from the electrocardiographic (ECG) signal.
 - a. The maximal heart rate ranges between 188 and 210 beats per minute. The mean maximal heart rates reported are virtually identical for boys and girls: 198 ± 11 for boys and 200 ± 9 for girls.
 - b. Heart rate declines abruptly during the first minute of recovery to between 140 and 150 beats per minute.

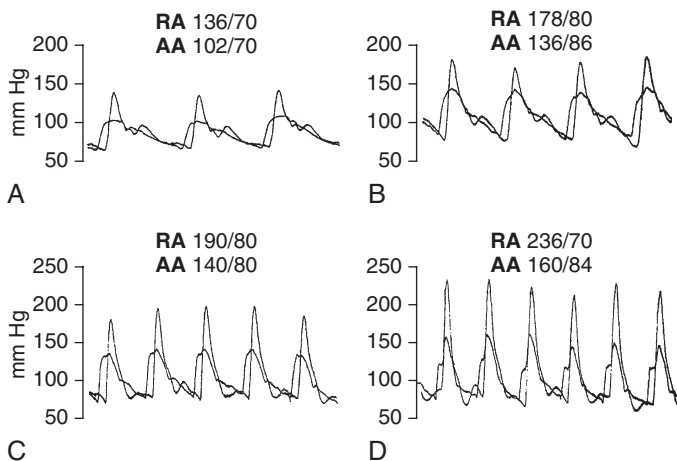
TABLE 5-1

PERCENTILES OF ENDURANCE TIME (MIN) BY BRUCE TREADMILL PROTOCOL

AGE GROUP (YR)	Percentiles					MEAN ± SD
	10	25	50	75	90	
BOYS						
4-5	6.8	7.0	8.2	10.0	12.7	8.9 ± 2.4
6-7	6.6	7.7	9.6	10.4	13.1	9.6 ± 2.3
8-9	7.0	9.1	9.9	11.1	15.0	10.2 ± 2.5
10-12	8.1	9.2	10.7	12.3	13.2	10.7 ± 2.1
13-15	9.6	10.3	12.0	13.5	15.0	12.0 ± 2.0
16-18	9.6	11.1	12.5	13.5	14.6	12.2 ± 2.2
GIRLS						
4-5	6.8	7.2	7.4	9.1	10.0	8.0 ± 1.1
6-7	6.5	7.3	9.0	9.2	12.4	8.7 ± 2.0
8-9	8.0	9.2	9.8	10.6	10.8	9.8 ± 1.6
10-12	7.3	9.3	10.4	10.8	12.7	10.2 ± 1.9
13-15	6.9	8.1	9.6	10.6	12.4	9.6 ± 2.1
16-18	7.4	8.5	9.5	10.1	12.0	9.5 ± 2.0

From Chatrath R, Shenoy R, Serratto M, Thoele DG: Physical fitness of urban American children, *Pediatric Cardiol* 23:608-612, 2002.

- c. Inadequate increments in heart rate may be seen with sinus node dysfunction, in congenital heart block, and after cardiac surgery.
- d. An extremely high heart rate at low levels of work may indicate physical decondition or marginal circulatory compensation.
3. **Blood pressure.** Blood pressure (BP) is measured in the arm with the auscultatory method or an oscillometric device. Accuracy of BP measurement is doubtful during exercise.
 - a. Systolic pressure increases linearly with progressive exercise. Systolic pressure usually rises to as high as 180 mm Hg with little change in diastolic pressure. Maximal systolic pressure in children rarely exceeds 200 mm Hg. During recovery it returns to baseline in about 10 minutes.
 - b. The diastolic pressure ranges between 51 and 76 mm Hg at maximum systolic blood pressure. Diastolic pressure also returns to the resting level by 8 to 10 minutes of recovery.
 - c. High systolic pressure in the arm, to the level of what is considered hypertensive emergency, raises a concern in both children and adults but it probably does not reflect the central aortic pressure. The major portion of the rise in arm systolic pressure during treadmill exercise probably reflects peripheral amplification due to vasoconstriction in the nonexercising arms (associated with increased blood flow to vasodilated exercising legs); central aortic pressure would probably be much lower than the systolic pressure in the arm in most cases. [Figure 5-1](#) is a dramatic illustration of a

**FIGURE 5-1**

Simultaneously recorded aortic and radial arterial pressure tracings in a young adult during rest (**A**) and those at 28.2% (**B**), 47.2% (**C**), and 70.2% (**D**) of maximal oxygen uptake during treadmill exercise. AA, ascending aorta; RA, radial artery. (From Rowell LB, Brengelmann GL, Blackmon JR, et al: *Circulation, Disparities between aortic and peripheral pulse pressure induced by upright exercise and vasomotor changes in man*, 37:954-964, 1968.)

relationship between the central and peripheral arterial pressures measured directly with arterial cannulas inserted in the ascending aorta and radial artery during upright exercise in young adults. Note that when the radial artery systolic pressure is over 230 mm Hg, the aortic pressure is only 160 mm Hg and there is very little increase in diastolic pressure. Therefore, the usefulness of arm BP in assessing CV function during upright exercise is questionable, except in the case of failure to rise.

- d. Failure of BP to rise to the expected level may be much more significant than the level of the rise in arm BP. The failure reflects an inadequate increase in cardiac output. This is commonly seen with cardiomyopathy, LVOT obstruction, coronary artery diseases, or the onset of ventricular or atrial arrhythmias.
4. **ECG monitoring.** The major reasons for ECG monitoring are to detect exercise-induced arrhythmias and ischemic changes.
 - a. Exercise-induced arrhythmias: Arrhythmias that increase in frequency or begin with exercise are usually significant. Type and frequency before and after the exercise and occurrence of new or more advanced arrhythmias should be noted. Occurrence of serious ventricular arrhythmias may be an indication to terminate the test.

- b. ST segment depression is the most common manifestation of exercise-induced myocardial ischemia.
 - (1) For children, down-sloping or sustained horizontal depression of the ST segment of 2 mm or greater when measured at 80 msec after the J point is considered abnormal (see Figure 2-20).
 - (2) Most guidelines for adult exercise testing consider ST segment depression of 1 mm or greater as an abnormal response. If the ST segment is depressed at rest, an additional depression of 1 mm or greater should be present to be significant.
 - (3) Specificity of the exercise ECG is poor in the presence of ST-T abnormalities on a resting ECG or with digoxin use.
 - (4) When there is an abnormal depolarization (such as BBB, ventricular pacemaker, or WPW preexcitation), interpretation of ST segment displacement is impossible.
5. **Oximetry.** Normal children maintain oxygen saturation greater than 90% during maximal exercise when monitored by pulse oximetry. Desaturation (<90%) is considered an abnormal response and may reflect pulmonary, cardiac, or circulatory compromise. Children who received lateral tunnel Fontan operation with fenestration may desaturate during exercise due to R-L shunt through the fenestration.

B. Indications for Exercise Stress Test

Common indications for exercise testing in children are as follows.

1. To evaluate specific signs or symptoms that are induced or aggravated by exercise
2. To assess or identify abnormal responses to exercise in children with cardiac, pulmonary, or other organ disorders, including the presence of myocardial ischemia and arrhythmias
3. To assess efficacy of specific medical or surgical treatments
4. To assess functional capacity for recreational, athletic, and vocational activities.
5. To evaluate prognosis, including both baseline and serial testing measurements
6. To establish baseline data for institution of cardiac, pulmonary, or musculoskeletal rehabilitation

C. Contraindications

1. Absolute contraindications include patients with acute myocardial or pericardial inflammatory diseases or patients with severe obstructive lesions in whom surgical intervention is clearly indicated.
2. Patients with pulmonary hypertension, documented long QT syndrome, uncontrolled hypertension, unstable arrhythmias, or Marfan syndrome and those who have had a heart transplantation are at high risk (and they may be relative contraindications).

D. Termination of Exercise Testing

1. Three general indications to terminate an exercise test are:
 - a. When diagnostic findings have been established and further testing would not yield any additional information;
 - b. When monitoring equipment fails; and
 - c. When signs or symptoms indicate that further testing may compromise the patient's well-being.
2. The following are some indications for termination of exercise testing in the pediatric age group.
 - a. Failure of heart rate to increase or a decrease in ventricular rate with increasing workload associated with symptoms (such as extreme fatigue, dizziness)
 - b. Progressive fall in systolic pressure with increasing workload
 - c. Severe hypertension, >250 mm Hg systolic or 125 mm Hg diastolic, or BP higher than can be measured by the laboratory equipment
 - d. Dyspnea that the patient finds intolerable
 - e. Symptomatic tachycardia that the patient finds intolerable
 - f. Progressive fall in oxygen saturation to <90% or a 10-point drop from resting saturation in a patient who is symptomatic
 - g. Presence of ≥ 3 mm flat or downward sloping ST segment depression
 - h. Increasing ventricular ectopy with increasing workload
 - i. Patient requests termination of the study

II. EXERCISE-INDUCED BRONCHOSPASM PROVOCATION TEST

Exercise in cold or dry air typically induces airway obstruction in asthmatic patients. Bronchial reactivity is measured while a subject exercises for 5 to 8 minutes on a treadmill at an intensity of 80% maximum capacity.

1. Baseline spirometry is obtained before exercise.
2. The exercise protocol used should increase the heart rate to 80% of predicted maximum within 2 minutes; starting with stage 4 of the Bruce protocol may be appropriate. The usual incremental workload used in many exercise tests is not appropriate, because if the intensity of exercise is raised slowly, the patient may develop refractoriness to bronchospasm.
3. Within 6 to 8 minutes of exercise or by the time the heart rate increases to 180 beats per minute, symptoms of airway obstruction develop.
4. Spirometry is repeated immediately after exercise and again at minute 5, 10, and 15 of recovery. Most pulmonary function test nadirs occur within 5 to 10 minutes after exercise.
5. Declines of 12% to 15% in FEV₁ are typically diagnostic.

III. LONG-TERM ECG RECORDING

Long-term ECG recording is the most useful method to document and quantitate the frequency of arrhythmias, correlate the arrhythmia with the patient's symptoms, and evaluate the effect of antiarrhythmic therapy.

A. Indications

Ambulatory ECG monitoring is obtained for the following reasons:

1. To determine whether symptoms such as chest pain, palpitation, or syncope are caused by cardiac arrhythmias
2. To evaluate the adequacy of medical therapy for an arrhythmia
3. To screen high-risk cardiac patients (such as those with hypertrophic cardiomyopathy or those in postoperative status after operations known to predispose to arrhythmias (e.g., Fontan-type operation))
4. To evaluate possible intermittent pacemaker failure in patients who have an implanted pacemaker
5. To determine the effect of sleep on potentially life-threatening arrhythmias

5

B. Types of Long-Term ECG Recorders

1. Holter recording
 - a. The Holter monitoring records the heart rhythm continuously for 24 hours, using ECG electrodes attached on the chest. The heart rhythm is recorded on a cassette tape or a flash card and then processed at a heart center. Two simultaneous channels are usually recorded to help distinguish artifacts from arrhythmias. The monitor has a built-in timer that is used with the patient's diary to allow subsequent correlation of symptoms and activities with arrhythmias. This type of recording is useful when the child has symptoms almost daily.
 - b. The following are suggested formats of interpretation of a 24-hour Holter recording.
 - (1) Describe the basic rhythm and the range of the heart rate.
 - (2) If there is bradycardia, describe its rate, rhythm, and duration (or number of beats) and the presence of escape beats, etc.
 - (3) For extreme tachycardia, describe the rate, rhythm, mode of initiation and termination, and its duration.
 - (4) Describe any abnormalities in AV conduction.
 - (5) Describe any arrhythmias, including their characteristics, duration, and frequency.
 - (6) Correlate the arrhythmias with the patient's activities and symptoms.
 - (7) If the patient complained of anginal pain, correlate ST segment changes with activities.
2. Event recorders: Event monitors are devices that are used by patients over a longer period (typically one month). The monitor is used when symptoms suggestive of an arrhythmia occur infrequently. Two general types of cardiac event monitors are available:
 - a. Looping memory (presymptom) event monitor. Two electrodes are attached on the chest. The monitor is always on but will store the patient's rhythm only when the patient or caregiver pushes the button. Most monitors will save the rhythm for 30 seconds before the device is activated.

- b. Nonlooping memory (postsymptom) event monitor. It does not have electrodes that are attached to the chest. This device is used to record symptoms that last longer than 45 to 60 seconds. It is a small device that has small metal discs that function as the electrodes. When symptoms occur, the device is pressed against the chest to start the recording. The device records and stores the events in solid-state memory. It can store up to 6 such events before it is necessary to transmit the information.
3. Implantable loop recorder: This device is indicated in patients with very infrequent symptoms, such as once every 6 months. Implantable loop recorders, about the size of a pack of chewing gum, are implanted beneath the skin in the upper left chest. The patient uses a hand-held activator to record and permanently store the cardiac rhythm when symptoms occur. The device can be “interrogated” through the skin to determine what the heart was doing when the symptoms occurred.

IV. AMBULATORY BLOOD PRESSURE MONITORING

Blood pressure is not a static variable; it changes not only from daytime to nighttime but also from minute to minute. In some patients, there is a transient elevation of BP when BP is measured in a health care facility (i.e., “white-coat hypertension”). This could lead to an overdiagnosis of hypertension and to unnecessarily aggressive and costly diagnostic studies and treatment. This test helps identify those with “white-coat hypertension.” Some researchers advocate the use of ambulatory BP monitoring (ABPM) in all patients with casual BP elevation.

A. Method of Ambulatory BP Monitoring

In ABPM, BP is measured multiple times with a preapplied BP cuff, usually using the oscillometric method for a 24-hour period while children participate in their normal daily activities, during both awake and sleep periods. Typically, BP measurements are programmed to occur every 15 to 30 minutes during awake periods and every 20 to 60 minutes during expected sleep periods. The use of ABPM is usually limited to children 5 to 6 years of age or older. Although the advantages of ABPM are clear, there are still some technical difficulties and problems with normative ambulatory BP levels in children.

B. Evaluation of Ambulatory BP Data

There are three basic calculations of ABPM.

1. The **mean BP value** can be determined for the entire 24-hour period or for awake and sleep periods separately. Mean normative ambulatory BP levels for children are shown in Table B-8 for boys and Table B-9 for girls in Appendix B.
2. Alternatively, the **BP load** can be calculated. BP load is the percentage of BP readings for a given period that exceeds the 95th percentile of normal for the individual patient. BP load in excess of 25% to 30% is typically considered elevated. Loads in excess of 50% may be predictive

TABLE 5-2

SUGGESTED SCHEME FOR STAGING OF AMBULATORY BP LEVELS IN CHILDREN

CLASSIFICATION	CLINIC BP	MEAN AMBULATORY SYSTOLIC BP	SYSTOLIC BP LOAD (%)
Normal BP	<95th percentile	<95th percentile	<25%
White-coat hypertension	>95th percentile	<95th percentile	<25%
Masked hypertension	<95th percentile	>95th percentile	>25%
Prehypertension	>95th percentile	<95th percentile	25-50%
Ambulatory hypertension	>95th percentile	>95th percentile	25-50%
Severe ambulatory hypertension (at risk for end-organ damage)	>95th percentile	>95th percentile	>50%

5

From Urbina E, Alpert B, Flynn J, et al: Ambulatory blood pressure monitoring in children and adolescents: Recommendations for standard assessment, *Hypertension* 52:433-451, 2008.

of LVH. Most experts use a combination of mean BP and BP load to categorize ABPM results as normal or abnormal (see [Table 5-2](#)).

3. **Nocturnal dipping.** Nocturnal dipping is calculated by subtracting the mean sleep BP from the mean awake BP and dividing this value by the mean awake BP.
 - a. Normal nocturnal dipping is at least 10% of mean awake BP.
 - b. Nondipping (defined as a decline of <10%) has been associated with hypertensive end-organ injury, end-stage renal disease, renal transplantation, or insulin-dependent diabetes mellitus. Black children have higher sleep BP levels and less significant decreases in BP during sleep compared with age-matched white counterparts.

C. Staging of Ambulatory BP Levels in Children

[Table 5-2](#) shows suggested staging of ambulatory BP levels in children and adolescents, recommended by a committee of the American Heart Association in 2008.

Chapter 6

Invasive Procedures

6

There are two kinds of invasive procedures that are used in the practice of pediatric cardiology: diagnostic cardiac catheterization (including angiocardiology) and catheter intervention procedures (therapeutic cardiac catheterization).

I. CARDIAC CATHETERIZATION AND ANGIOCARDIOGRAPHY

Cardiac catheterization and angiocardiology are the definitive diagnostic tests for most cardiac patients. They are carried out under sedation or anesthesia.

A. Indications

Accurate diagnosis of most CHDs does not require diagnostic catheterization. With improved capability of noninvasive imaging tools such as echo and color flow Doppler studies and radiologic techniques such as cardiac MRI and cardiac CT, many cardiac problems are adequately diagnosed and managed without cardiac catheterization studies. Indications for these invasive studies vary from institution to institution and from cardiologist to cardiologist. In most centers, two thirds of the cardiac catheterizations are for interventional purposes and only one third are for diagnostic purposes. The following are some circumstances that suggest the need for diagnostic catheterization.

1. To perform balloon procedures for angioplasty (with or without stent placement), valvuloplasty, or balloon atrial septostomy in patients with lesions amenable to these procedures
2. To determine accurate pressure gradients in combined lesions of AS and AR or PS and PR, or multiple levels of obstruction
3. To assess pulmonary hypertension and its responsiveness to vasodilator therapy
4. To calculate pulmonary vascular resistance in the setting of low-flow lesions, such as seen in patients after bidirectional Glenn operation or after complete Fontan operation
5. To determine details of pulmonary vascular supply, the aortopulmonary collateral supply, and the coronary artery anatomy in patients with pulmonary atresia with intact ventricular septum or pulmonary atresia with complex ventricular anatomy
6. To find answers to postoperative problems such as excessive desaturation after a B-T shunt or bidirectional Glenn operation, or when excessive aortopulmonary collateral is suspected
7. To assess post-transplantation vasculopathy and to obtain endomyocardial biopsy for rejection identification in cardiac transplantation patients

8. To assess cardiomyopathy or myocarditis
9. To assess coronary circulation in some cases of Kawasaki disease

B. Sedation

The following sedatives have been used singly or in combination by different institutions with equally good success rates. In general, smaller doses of sedatives are used in cyanotic infants.

1. General anesthesia is often used in newborns and cyanotic infants.
2. For infants less than 10 kg, a combination of chloral hydrate, 75 mg/kg (maximum 2 g) PO, and diphenhydramine, 2 mg/kg (maximum 100 mg) PO, has been used with good results.
3. For older children, Demerol compound, a solution containing 25 mg/mL of meperidine (Demerol), 12.5 mg/mL of promethazine (Phenergan), and 12.5 mg/mL of chlorpromazine (Thorazine), is popular. The dose of the Demerol compound is 0.11 mL/kg IM. Some centers exclude chlorpromazine from the mixture. In cyanotic children, the dose is reduced by one third. For children with severe CHF, the dose is reduced by half.
4. A combination of meperidine 1 mg/kg and hydroxyzine (Vistaril) 1 mg/kg IM, or of fentanyl 1.25 µg/kg and droperidol 62.5 µg/kg IM gives an equally good result.
5. Ketamine, 3 mg/kg IM or 1 to 2 mg/kg IV, may be used, but it can change the hemodynamic data because it increases the systemic vascular resistance and blood pressure.
6. Morphine 0.1 to 0.2 mg/kg administered subcutaneously has been used in cyanotic infants to prevent or treat hypoxic spells.
7. If more sedation is required during the study, intravenous diazepam (Valium), 0.1 mg/kg, or morphine, 0.1 mg/kg, is used.

C. Hemodynamic Values and Their Calculations

Pressure and oxygen saturation values for normal children are shown in Figure 6-1. During cardiac catheterization, cardiac output, cardiac shunt, and vascular resistance are routinely calculated.

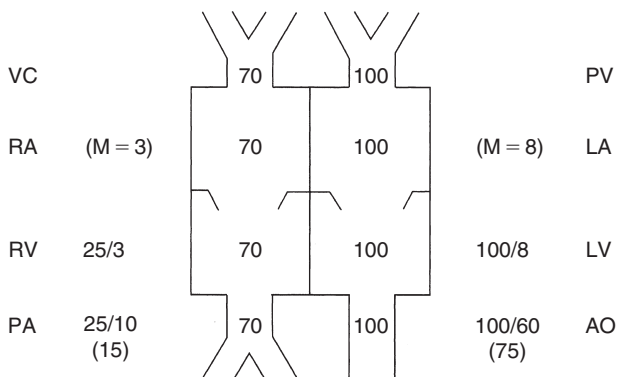
1. **Flows (cardiac output)** are calculated by the Fick formula:

$$\text{Pulmonary flow (Qp)} = \frac{\text{VO}_2}{\text{C}_{\text{PV}} - \text{C}_{\text{PA}}}$$

$$\text{Systemic flow (Qs)} = \frac{\text{VO}_2}{\text{C}_{\text{AO}} - \text{C}_{\text{MV}}}$$

where flows are in liters per minute, VO_2 is oxygen consumption in milliliters per minute, and C is oxygen content in milliliters per liter at the various positions: the pulmonary vein (PV), pulmonary artery (PA), aorta (AO), and mixed systemic venous blood (MV).

Oxygen consumption is either directly measured during the procedure or estimated from a table (see Appendix, Table A-6). Oxygen content

**FIGURE 6-1**

Average values of pressure and oxygen saturation in normal children. AO, aorta; LA, left atrium; LV, left ventricle; M, mean pressure; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; VC, vena cava.

(milliliters per 100 mL of blood) is derived by multiplying oxygen capacity by percent saturation. Oxygen capacity (milliliters per 100 mL of blood) is the total content of oxygen that hemoglobin contains when it is 100% saturated ($1.36 \times$ hemoglobin in grams per 100 mL). Normal systemic flow (or pulmonary flow in the absence of shunt) is 3.1 ± 0.4 L/min/m² (i.e., cardiac index).

2. **The magnitude of the shunt** is calculated as follows:

$$\text{Left-to-right (L-R) shunt} = Q_p - Q_s$$

$$\text{Right-to-left (R-L) shunt} = Q_s - Q_p$$

In pediatrics, the ratio of pulmonary to systemic flow (Q_p/Q_s), which does not require an oxygen consumption value, is often used. The ratio provides information on the magnitude of the shunt. Patients with an L-R shunt greater than 2:1 are usually candidates for surgery.

3. **Vascular resistances** are calculated by using formulas derived from Ohm's law ($R = \Delta P/Q$).

$$\text{PVR} = \frac{\text{Mean PA pressure} - \text{mean LA pressure}}{Q_p}$$

$$\text{SVR} = \frac{\text{Mean aortic pressure} - \text{mean RA pressure}}{Q_s}$$

The normal systemic vascular resistance (SVR) varies between 15 and 30 units/m². The normal pulmonary vascular resistance (PVR) is high at

birth but reaches near-adult values (1 to 3 units/m²) after 2 to 4 months. The normal ratio of PVR/SVR ranges from 1:20 to 1:10.

D. Selective Angiocardiology

A radiopaque dye is rapidly injected through a cardiac catheter into a certain site in the cardiovascular system, and angiograms are obtained, often on biplane views. Nonionizing contrast media with low osmolality (e.g., Isovue, Omnipaque) are widely used because of their low incidence of side effects. The dose of angiographic dyes for an angiogram ranges from 1 to 2 mL/kg of body weight, depending on the nature of the defect.

E. Risks

1. The risk of cardiac catheterization and angiocardiology varies with the age and illness of the patient, the type of lesion, and the experience of those doing the procedure. Serious complications can occur, including (rarely) death. The reported rate of fatal complications varies from less than 1% to as high as 5% in neonates. About 3% to 5% of patients have significant nonfatal complications.
2. Complications include serious arrhythmias, heart block, cardiac perforation, hypoxic spells, arterial obstruction, hemorrhage, infection, reactions to the contrast material, intramyocardial injection of the contrast, and renal complications (hematuria, proteinuria, oliguria, and anuria). Hypothermia, acidemia, hypoglycemia, convulsions, hypotension, and respiratory depression are more likely in the newborn infant.

F. Preparation and Monitoring

Adequate preparation of the patient and careful monitoring during the procedure can minimize complications and fatality from the invasive studies. The following areas are particularly important.

1. Avoiding hypothermia when an infant is being studied, by increasing temperature in the cardiac catheterization laboratory, using a warming blanket, and monitoring rectal temperature.
2. Monitoring oxygen saturation transcutaneously, checking arterial blood gases and pH, and correcting acidemia and hypoxemia; correcting hypoglycemia or hypocalcemia before the start of the procedure.
3. Administering oxygen, if indicated, during the procedure.
4. Intubating or readiness for intubating in infants with respiratory difficulties, and having emergency medications (e.g., atropine, epinephrine, bicarbonate) drawn up and ready.
5. Initiating prostaglandin infusion in cyanotic infants who appear to have a ductus-dependent lesion.
6. Whenever possible, having another physician or an anesthesiologist available to monitor the patient.

II. CATHETER INTERVENTION PROCEDURES

Catheter interventional procedures can save lives of critically ill neonates and may eliminate or delay the need for elective surgical procedures. Blood vessels and heart valves that are too small can be enlarged using balloon catheters and/or implantable stents. Too small an opening in the atrial septum can be enlarged by using balloon or blade catheters. An opening can be created in an intact atrial septum for left-to-right or right-to-left shunt to occur. Abnormal connections within the heart (such as ASD and VSD) can be closed using innovative devices. Abnormal blood vessels (PDA or collaterals) can also be closed using coils or plugging devices. In recent years, percutaneous valve replacement in the aortic or pulmonary position has seen wider use.

A. Atrial Septostomy

In balloon atrial septostomy (Rashkind's procedure), an opening is created or enlarged in the atrial septum, using a special balloon-tipped catheter, to improve shunting at the atrial level in patients with serious CHDs (such as TGA, pulmonary atresia, tricuspid atresia, TAPVR, etc.). In infants older than 6 to 8 weeks of age, the atrial septum may be too thick to allow an effective balloon septostomy. In such cases, the atrial septum can be opened using a blade catheter (i.e., Park blade). The opening can then be torn further with a balloon catheter.

B. Balloon Valvuloplasty

The balloons used in this interventional procedure are made of special plastic polymers and retain their predetermined diameters.

1. **Pulmonary valve stenosis.** Balloon pulmonary valvuloplasty is the treatment of choice for valvular pulmonary stenosis (PS) in children and, to a large extent, has replaced the surgical pulmonary valvotomy. Balloon valvuloplasty may be indicated in patients with a resting systolic pressure gradient of ≥ 40 mm Hg under sedation in the cardiac catheterization laboratory.
2. **Aortic valve stenosis.** This procedure is more difficult and carries a higher complication rate than does pulmonary valvuloplasty, especially for infants. The gradient reduction is less effective than for the pulmonary valve. Balloon valvuloplasty may be indicated in children with isolated valvular AS with a resting peak-to-peak systolic gradient of ≥ 50 mm Hg (without significant AR) by cardiac catheterization. The procedure is also indicated in newborns with isolated critical valvular AS that is ductal dependent. Complications include production or worsening of AR, iliofemoral artery injury and occlusion, ventricular arrhythmias, and even death in small infants.
3. **Mitral stenosis.** Balloon dilatation valvuloplasty has been effective for rheumatic mitral stenosis (MS) but less effective for congenital MS.
4. **Stenosis of prosthetic conduits and valves within conduits.** The balloon dilatation procedure may reduce the transconduit gradient across stenotic areas of prosthetic conduits and across valves contained within conduits.

C. Balloon Angioplasty

Balloon catheters similar to those used in balloon valvuloplasties are used for the relief of stenosis of blood vessels. This procedure has been used for coarctation of the aorta, pulmonary artery branch stenosis, and stenosis of the systemic veins. Following the balloon procedure, some blood vessels recoil and do not maintain the dilated caliber of the vessel. Endovascular stents are sometimes used to maintain vessel patency after balloon angioplasty of any vascular structure. After stent placement, the vascular endothelium grows over the struts of the stent over several months, functionally incorporating the stent into the vessel wall. Occasionally, however, the endothelialization may go awry, resulting in a thick neointimal layer causing a functional stenosis.

1. **Recoarctation of the aorta.** Balloon angioplasty has become the procedure of choice for patients with postoperative residual obstruction of coarctation of the aorta. Some centers use a stent to prevent restenosis.
2. **Native (or unoperated) coarctation of the aorta.** Balloon angioplasty for native unoperated coarctation is controversial. The rate of recoarctation following the balloon procedure appears higher than that following surgery in infants. The complication rate is 17%, with aortic aneurysm formation (both acute and late) occurring in 6% of the patients. The long-term effects of the procedure on aneurysm formation are unknown. Some centers use cutting balloons or low-profile stents in very sick infants, which may reduce aneurysm formation.
3. **Branch pulmonary artery stenosis.** Surgical treatment of peripheral PA stenosis is often impossible. Hypoplastic and stenotic branch PAs are seen with postoperative TOF, pulmonary atresia, and HLHS. The immediate success rate of the balloon procedure is about 60%, but restenosis occurs in a significant number of patients, and aneurysm formation occurs in approximately 3% of patients. High-pressure balloons appear to improve the effectiveness. Vessels resistant to high-pressure balloon respond to either cutting balloon angioplasty alone or followed by high-pressure ballooning. Cutting balloons have 3 or 4 microsurgical blades with a cutting depth of 0.15 mm, which are activated when the balloons are inflated. Use of an intravascular stent has also improved immediate results and may improve the long-term success rate.
4. **Systemic venous stenosis.** The balloon procedure may be performed for obstructed venous baffles after the Senning operation for TGA.

D. Closure Techniques

Various closure devices have been used for nonsurgical closure of ASD, PDA, and muscular VSD in the cardiac catheterization laboratory.

1. Atrial septal defect.
 - a. There are several devices available, some approved by the U.S. Food and Drug Administration (FDA) and others in clinical trial stages. In the United States, currently the Amplatzer septal occlude (AGA Medical) and Helex septal occlude (W. LO. Gore and Associates) are approved for closure of secundum ASD.

- b. The use of the closure device may be indicated to close a secundum ASD measuring 5 mm or more in diameter (but less than 32 mm for the Amplatzer device and less than 18 mm for the Helex device), and there must be at least a 4 mm rim of atrial septal tissue around the defect. After the device closure, patients take a baby aspirin daily for 6 months until endothelialization of the device is complete.
2. Ventricular septal defect. Successful closure of a muscular VSD, which is remote from cardiac valves, has been reported by using the double-umbrella clamshell device and others.
3. Patent ductus arteriosus.
 - a. Most transcatheter PDA closures are now performed using Gianturco vascular occlusion coils. They are small, coiled wires coated with thrombogenic Dacron strands that open like a small “pigtail” when placed in the vessel. Good candidates for the coil occlusion are those children weighing 6 kg and larger with the ductus 4 mm and smaller.
 - b. For larger PDA (but less than 12 mm in diameter), specialized devices such as the Amplatzer duct occluder are available for catheter-based closure. The devices are implanted antegrade from the femoral vein. There is a $\geq 98\%$ closure rate at 6 months with minimal complications and no mortality. Very large ducts in small infants are still probably best treated surgically.
4. Occlusion of collaterals and other vessels. This technique closes aortopulmonary collaterals (often seen with TOF), systemic arteriovenous fistulas, pulmonary arteriovenous fistulas, or surgically placed shunts that are no longer needed. The Gianturco coil and the White balloon are examples. Peripheral embolization of the coil or balloon into the PAs or the aorta is a major risk.

E. Percutaneous Valve Placement

Since Bonhoeffer and his colleagues first replaced pulmonary valves by percutaneous techniques in 2000, this technique has gained increasing experience. Candidates for this technique are typically those patients who received surgery for tetralogy of Fallot and late development of severe pulmonary regurgitation. This technique is expected to reduce the need for repeated cardiac surgeries by replacing surgically placed conduits. Most of the reported cases used the Melody transcatheter pulmonary valve (Medtronic, Minneapolis, MN). The Edwards SAPIEN valve (Edwards Lifescience, Irvine, CA) is a new valve with which experience is very limited.

CONGENITAL HEART DEFECTS

Congenital heart defects will be divided into the following four topics: left-to-right shunt lesion, obstructive lesions, cyanotic heart defects, and miscellaneous congenital heart defects.

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Chapter 7

Left-to-Right Shunt Lesions

I. ATRIAL SEPTAL DEFECT (OSTIUM SECUNDUM ASD)

A. Prevalence

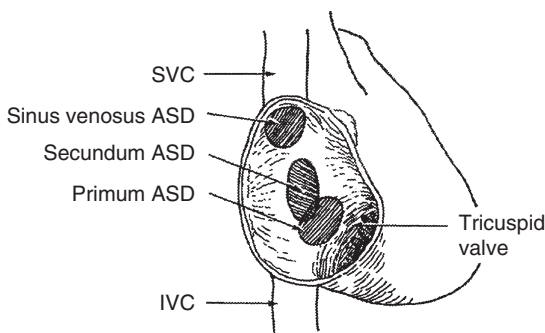
5% to 10% of all congenital heart diseases (CHDs). Female preponderance (male to female ratio of 1:2).

B. Pathology and Pathophysiology

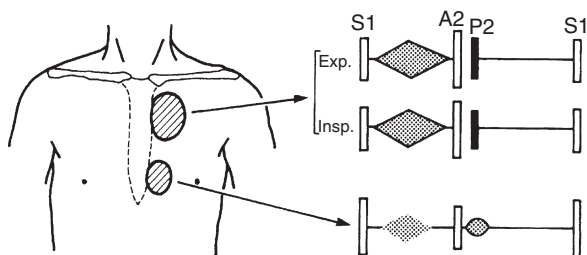
1. Three types of atrial septal defects (ASDs) occur in the atrial septum (Fig. 7-1).
 - a. Secundum ASD is in the central portion of the septum and is the most common type (50% to 70% of ASDs).
 - b. Primum ASD (or partial endocardial cushion defect [ECD]) is in the lower part of the septum (30% of ASDs).
 - c. Sinus venosus defect is near the entrance of the SVC or IVC to the RA (about 10% of all ASDs). PAPVR is common with a sinus venous defect.
2. An L-R shunt occurs through the defect, with a volume overload to the RA and RV and an increase in pulmonary blood flow.

C. Clinical Manifestations

1. The patients are usually asymptomatic.
2. A widely split and fixed S2 and a grade 2 to 3/6 systolic ejection murmur at the ULNB are characteristic of moderate-size ASD (Fig. 7-2). With a large L-R shunt, a mid-diastolic rumble (resulting from relative TS) may be audible at the LLNB. The typical auscultatory findings are usually absent in infants and toddlers, even in those with a large defect, because the RV is not compliant enough to result in a large L-R shunt in these patients.
3. The ECG shows RAD (+90 to +180) and mild RVH, RBBB, or IRBBB with an rsR' pattern in V1.
4. Chest radiographs show cardiomegaly (with RAE and RVE), increased PVM, and a prominent MPA segment when the shunt is moderate or large.
5. Two-dimensional echo shows the position and the size of the defect. Cardiac catheterization is not necessary.
6. Natural history.
 - a. Spontaneous closure of the defect occurs in more than 80% of patients with defects of 3 to 8 mm (diagnosed by echo) before 1½ years of age.
 - b. An ASD with a diameter >8 mm rarely closes spontaneously. Spontaneous closure is not likely to occur after 4 years of age. The defect may reduce in size in some patients.
 - c. Spontaneous closure does not occur in primum or sinus venous type.

**FIGURE 7-1**

Anatomic types of atrial septal defect (ASD) viewed with the right atrial wall removed. IVC, inferior vena cava; SVC, superior vena cava. (From Park MK, *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

**FIGURE 7-2**

Cardiac findings of ASD. Throughout this book, heart murmurs *with solid borders* are the primary murmurs, and those *without solid borders* are transmitted murmurs or those occurring occasionally. Abnormalities in heart sounds are shown in *black*. Exp., Expiration; Insp., inspiration. (From Park MK, *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- d. If the defect is large and left untreated, pulmonary hypertension develops in the third and fourth decades of life.
- e. Cerebrovascular accident due to paradoxical embolization through an ASD is possible.

D. Management

Medical

1. Exercise restriction is not required, unless symptomatic.
2. Nonsurgical closure of the defect using a catheter-delivered closure device has become a preferred method, provided the indications are met.

- a. These devices are applicable only to secundum ASD. The use of the closure device may be indicated for a defect measuring ≥ 5 mm in diameter (but less than 32 mm for Amplatzer device and less than 18 mm for Helex device) with evidence of RA and RV volume overload.
- b. In the United States, currently the Amplatzer septal occluder (AGA Medical) and Helex septal occluder (W. L. Gore and Associates) are approved for secundum ASD closure.
- c. There must be enough rim (4 mm) of septal tissue around the defect for appropriate placement of the device.
- d. The size of the rim around the ASD can be estimated by 2D echo study as diagrammatically shown in [Figure 7-3](#). The rim size is estimated in four directions: anterosuperior, anteroinferior, posteroinferior, and posteroinferior.
- e. The ASD devices can be implanted successfully in children younger than 2 years of age, although a weight >15 kg is preferred.
- f. Following the device closure, the patients are placed on aspirin 81 mg per day for 6 months.

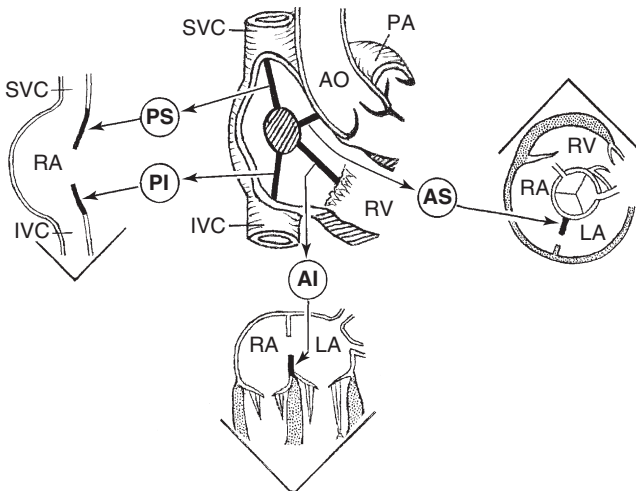


FIGURE 7-3

2D echo estimates of the ASD rim size. The posteroinferior (PS) and posteroinferior (PI) rims are estimated in the bi-vena caval view from the subcostal transducer position, the anteroinferior (AI) rim from the apical four-chamber view, and the anterosuperior (AS) (or retro-aortic) rim from the parasternal short-axis view. AO, aorta; IVC, inferior vena cava; LA, left atrium; PA, pulmonary artery; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

- g. Advantages of nonsurgical closure would include a less-than-24-hour hospital stay, rapid recovery, and no residual thoracotomy scar.
- h. Closure rates are excellent with small residual shunts seen in less than 5% at 1-year follow-up.

Surgical

For patients with primum ASD and sinus venosus defect, and some patients with secundum ASD for which the device closure is considered inappropriate, surgical closure is indicated when there is a significant L-R shunt with Qp/Qs of 1.5:1 or greater. Surgery is usually delayed until 2 to 4 years of age, unless CHF develops. Open repair with a midsternal incision or minimally invasive cardiac surgical technique (with a smaller skin incision) is used. The surgical mortality rate is less than 1%. High PVR (≥ 10 units/m²) is a contraindication to surgery.

Follow-Up

1. Periodic follow-up is needed after the ASD closure device implantation for residual shunt, obstruction of pulmonary and systemic venous returns, and interference with the AV valve function.
2. After surgery, atrial or nodal arrhythmias occur in 7% to 20% of patients. Occasional sick sinus syndrome requires pacemaker therapy.

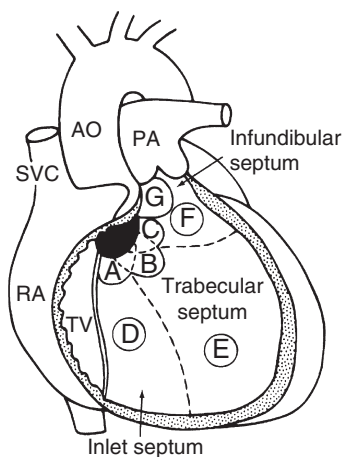
II. VENTRICULAR SEPTAL DEFECT

A. Prevalence

VSD is the most common form of CHD, accounting for 15% to 20% of all CHDs, not including those occurring as part of cyanotic CHDs.

Pathology and Pathophysiology

1. The ventricular septum consists of a small membranous septum and a larger muscular septum. The muscular septum has three components: the inlet, infundibular, and trabecular (or simply muscular) septa ([Fig. 7-4](#)).
2. A membranous VSD often involves a varying amount of muscular septum adjacent to it (i.e., perimembranous VSD). The perimembranous defect is more common (70%) than the trabecular (5% to 20%), infundibular (5% to 7%), or inlet defects (5% to 8%). In the Far Eastern countries, the infundibular defects account for about 30%. The perimembranous VSD is frequently associated with PDA and COA.
3. The VSD seen with TOF is a large nonrestrictive perimembranous defect with extension into the subpulmonary region.
4. The inlet VSD is typically seen with endocardial cushion defects.
5. In subarterial infundibular or supracristal VSD, the aortic valve may prolapse through the VSD, with resulting AR and reduction of the VSD shunt. The prolapse may occasionally occur with the perimembranous VSD.
6. In VSDs with small to moderate L-R shunts, volume overload is placed on the LA and LV (but not on the RV). With larger defects the RV is also under volume and pressure overload, in addition to a greater

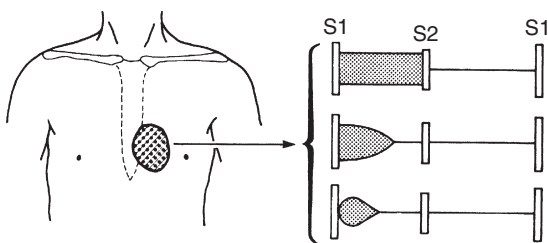
**FIGURE 7-4**

Anatomic locations of various types of VSD, viewed with the RV free wall removed. Black area is the membranous ventricular septum. **A**, Perimembranous inlet (“AV canal-type”) VSD; **B**, perimembranous trabecular (typical membranous) VSD; **C**, perimembranous infundibular (“tetralogy-type”) VSD; **D**, inlet muscular VSD; **E**, trabecular muscular VSD; **F**, infundibular or outlet muscular VSD; **G**, subarterial infundibular (supracristal) VSD. AO, aorta; PA, pulmonary artery; RA, right atrium; SVC, superior vena cava; TV, tricuspid valve.

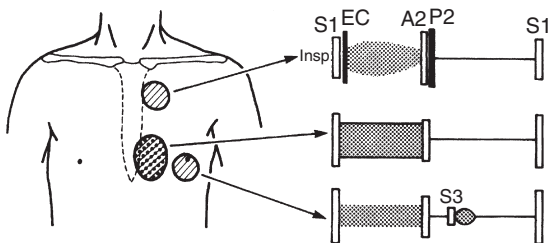
volume overload on the LA and LV. PBF is increased to a varying degree depending on the size of the defect and the pulmonary vascular resistance. With a large VSD, pulmonary hypertension results. With a long-standing large VSD, pulmonary vascular obstructive disease (PVOD) develops, with severe pulmonary hypertension and cyanosis resulting from an R-L shunt. At this stage, surgical correction is nearly impossible.

Clinical Manifestations

1. Patients with small VSDs are asymptomatic, with normal growth and development. With large VSDs, delayed growth and development, repeated pulmonary infections, CHF, and decreased exercise tolerance are relatively common. With PVOD, cyanosis and a decreased level of activity may result.
2. With a small VSD, a grade 2 to 5/6 regurgitant systolic murmur (holosystolic or less than holosystolic) maximally audible at the LLSB is characteristic (Fig. 7-5). A systolic thrill may be present at the LLSB. With a large defect, an apical diastolic rumble is audible, which represents a relative stenosis of the mitral valve due to large pulmonary

**FIGURE 7-5**

Cardiac findings of a small VSD. A regurgitant systolic murmur is best audible at the LLSB; it may be holosystolic or less than holosystolic. Occasionally, the heart murmur is in early systole. A systolic thrill may be palpable at the LLSB (*dots*). The S2 splits normally, and the P2 is of normal intensity.

**FIGURE 7-6**

Cardiac findings of a large VSD. A classic holosystolic regurgitant murmur is audible at the LLSB. A systolic thrill is also palpable at the same area (*dots*). There is usually a mid-diastolic rumble, resulting from relative MS, at the apex. The S2 is narrowly split, and the P2 is accentuated in intensity. Occasionally an ejection click (*EC*) may be audible in the ULSB when associated with pulmonary hypertension. The heart murmurs shown without solid borders are transmitted from other areas and are not characteristic of the defect. Abnormal sounds are shown in *black*.

venous return to the LA (Fig. 7-6). The S2 may split narrowly, and the intensity of the P2 increases if pulmonary hypertension is present (Fig. 7-6).

- ECG findings: Small VSD, normal; moderate VSD, LVH and LAH (\pm); large VSD, biventricular hypertrophy (BVH) and LAH (\pm); PVOD, pure RVH.
- Chest radiographs reveal cardiomegaly of varying degrees with enlargement of the LA, LV, and possibly the RV. Pulmonary vascular markings (PVMs) are increased. The degree of cardiomegaly and the increase in PVMs are directly related to the magnitude of the L-R shunt. In PVOD, the heart is no longer enlarged and the MPA and the hilar pulmonary arteries are notably enlarged, but the peripheral lung fields are ischemic.

5. Two-dimensional echo studies provide accurate diagnosis of the position and size of the VSD. LA and LV dimensions provide indirect assessment of the magnitude of the shunt. Figure 7-7 shows diagrams of 2D echo views of different parts of the ventricular septum, which helps identify different types of VSDs. The Doppler studies of the PA, TR (if present), and the VSD itself are useful in indirect assessment of RV and PA pressures (see Doppler echocardiography in Chapter 4).
6. Natural history.
 - a. Spontaneous closure occurs in 30% to 40% of all VSDs, most often in small trabecular VSDs, more frequently in small defects than in large defects, and more often in the first year of life than thereafter.
 - b. Large defects tend to become smaller with age.
 - c. Inlet and infundibular VSDs do not become smaller or close spontaneously.
 - d. CHF develops in infants with a large VSD but usually not until 6 or 8 weeks of age, when the PVR drops below a critical level.
 - e. PVOD may begin to develop as early as 6 to 12 months of age in patients with a large VSD.

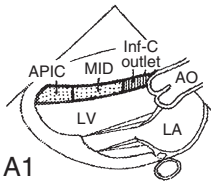
B. Management

Medical

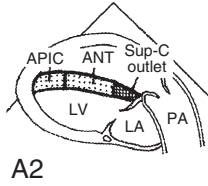
1. Treatment of CHF with diuretics, after-load reducers, and sometimes digoxin (see Chapter 19).
2. No exercise restriction is required in the absence of pulmonary hypertension.
3. Nonsurgical device closure of selected muscular VSDs is possible when the defect is not too close to cardiac valves and when it is difficult to access surgically. Some centers have used so-called hybrid procedures through left thoracotomy incision and performing “perventricular” device closure without the use of cardiopulmonary bypass to close muscular VSD. Device closure is not popular for the perimembranous VSD because of the unacceptable rate of postprocedure heart block.

Surgical

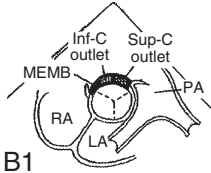
1. Procedure.
 - a. Direct closure of the defect is performed under cardiopulmonary bypass, preferably through an atrial approach rather than through a right ventriculotomy.
 - b. PA banding is rarely performed unless additional lesions make the complete repair difficult.
2. Indications and timing.
 - a. A significant L-R shunt with Qp/Qs of greater than 2:1 is an indication for surgical closure. Surgery is not indicated for a small VSD with Qp/Qs less than 1.5:1.



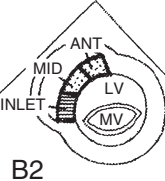
A1



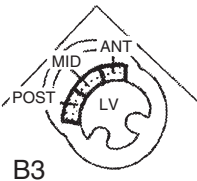
A2



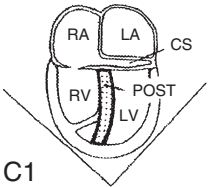
B1



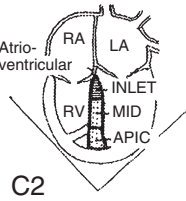
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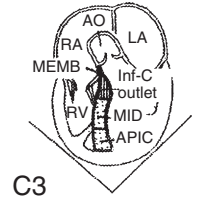
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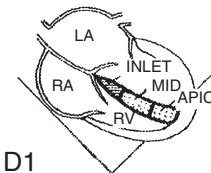
C1



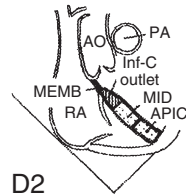
C2



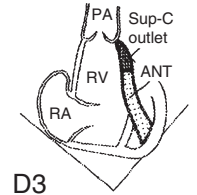
C3



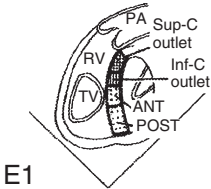
D1



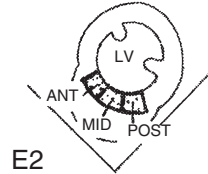
D2



D3



E1



E2



- b. Timing.
 - (1) Infants with CHF and growth retardation unresponsive to medical therapy should be operated on at any age, including early infancy.
 - (2) Infants with a large VSD and evidence of increasing PVR should be operated on as soon as possible.
 - (3) Infants who respond to medical therapy may be operated on by the age of 12 to 18 months.
 - (4) Asymptomatic children may be operated on between 2 and 4 years of age.
 - c. Contraindications. PVR/SVR ratio of 0.5 or greater or PVOD with a predominant R-L shunt.
3. Surgical approaches for special situations.
- a. **VSD + large PDA.** If the PDA is large, the ductus alone may be closed in the first 6 to 8 weeks, and the VSD may be closed later. If the VSD is large and nonrestrictive, the VSD should be closed early and the PDA ligated at the time of VSD repair.
 - b. **VSD + COA.** Controversies exist. One approach is the repair of COA alone initially and the closure of the VSD later if indicated. Other options include COA repair and PA banding if the VSD appears large or repair of both defects at the same time using one or two incisions.
 - c. **VSD + AR** is usually associated with subarterial infundibular (or supracristal) VSD and occasionally with perimembranous VSD. When AR is present, a prompt closure of the VSD is recommended, even if the Qp/Qs is less than 2:1, to abort progression of or to abolish AR. Some centers close VSD if aortic prolapse is evident even in the absence of AR.

Follow-Up

Postoperatively, an office follow-up should be done every 1 to 2 years. The ECG shows RBBB in 50% to 90% of the patients who had VSD repair through right ventriculotomy and in up to 40% of the patients who had repair through the right atrial approach.

FIGURE 7-7

Selected 2D echo views of the ventricular septum. These schematic drawings are helpful in determining the type of VSD. Different shading has been used for easy recognition of different parts of the ventricular septum. Row **A**, parasternal long-axis views; Row **B**, parasternal short-axis views; Row **C**, apical four- and “five-chamber” views; Row **D**, subcostal long-axis views; and Row **E**, subcostal short-axis views. ANT, anterior muscular; AO, aorta; APIC, apical muscular; CS, coronary sinus; Inf-C outlet, infracristal outlet muscular; INLET, inlet muscular; LA, left atrium; LV, left ventricle; MEMB, membranous; MID, mid-muscular; PA, pulmonary artery; POST, posterior muscular; RA, right atrium; RV, right ventricle; Sup-C outlet, supracristal outlet muscular. (From Park MK: *Park’s Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

III. PATENT DUCTUS ARTERIOSUS

A. Prevalence

5% to 10% of all CHDs, excluding those in premature infants. PDA in premature infants is presented under a separate heading.

B. Pathology and Pathophysiology

1. There is a persistent postnatal patency of a normal fetal structure between the PA and the descending aorta.
2. The magnitude of the L-R shunt is determined by the diameter and length of the ductus and the level of PVR. With a long-standing large ductus, pulmonary hypertension and PVOD may develop with an eventual R-L shunt and cyanosis.

C. Clinical Manifestations

1. The patients are asymptomatic when the ductus is small. When the defect is large, signs of CHF may develop.
2. A grade 1 to 4/6 continuous (machinery) murmur best audible at the ULSC or left infraclavicular area is the hallmark of the condition (Fig. 7-8). An apical diastolic rumble is audible with a large-shunt PDA. Bounding peripheral pulses with wide pulse pressure are present with a large-shunt PDA.
3. ECG findings are similar to those of VSD: normal or LVH in a small to moderate PDA; BVH in a large PDA; RVH if PVOD develops.
4. Chest radiographs are also similar to those of VSD: normal with a small-shunt PDA; with a large-shunt PDA, cardiomegaly (with LA and LV enlargement) and increased PVM are present; with PVOD the heart size is normal, with a marked prominence of the MPA and hilar vessels.
5. The PDA can be directly imaged and its hemodynamic significance determined by 2D echo and color flow Doppler examination. Cardiac catheterization is not indicated in isolated PDA.
6. CHF or recurrent pneumonia or both develop if the shunt is large. Spontaneous closure of PDA usually does not occur in term infants.

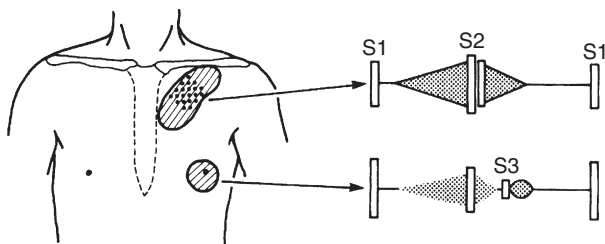


FIGURE 7-8

Cardiac findings of PDA. A continuous murmur, maximally audible at the LUSB or left infraclavicular area, is a typical finding. When the shunt is large, a diastolic rumble is audible at the apex. A systolic thrill may be present in the area shown by dots.

D. Management

Medical

1. No exercise restriction is required in the absence of pulmonary hypertension.
2. Indomethacin is ineffective in term infants with PDA.
3. Indications for nonsurgical closure of PDA:
 - a. Definitely indicated for hemodynamically significant PDA with CHF, failure to thrive, or enlarged LA and LV.
 - b. Reasonable to close small PDA when the murmur of PDA is audible.
 - c. Controversial for closing so-called silent ductus, which is a small ductus incidentally detected by echo studies but without audible heart murmur.
 - d. Contraindicated when PVOD is present.
4. Catheter closure of the ductus may be employed. Small ductus <4 mm in diameter are closed by Gianturco stainless coils and larger ones by Amplatzer PDA device. An optimal candidate for the coil occlusion has the ductus 2.5 mm or less in size but the use of multiple coils can close a ductus up to 5 mm. Amplatzer device may be used for PDAs ranging in size from 4 to 10 mm (with 100% closure rate). Complications may include residual leaks, pulmonary artery coil embolization, hemolysis, left PA stenosis, aortic occlusion with the Amplatzer device, and femoral vessel occlusion.

Surgical

Surgical closure is reserved for those patients in whom nonsurgical closure technique is not considered applicable. Ligation and division through left posterolateral thoracotomy without cardiopulmonary bypass is performed. Repair through a smaller incision with video-assisted thoracoscopy is becoming popular. Surgical mortality is near 0%. PVOD is a contraindication to surgery.

E. Differential Diagnosis

The following conditions require differentiation from PDA because they may present with a heart murmur similar to that of PDA and/or with bounding pulses.

1. Coronary AV fistula (the murmur is audible over the precordium, not at the ULSB).
2. Systemic AV fistula (a wide pulse pressure with bounding pulse, CHF, and a continuous murmur over the fistula [head or liver] are characteristic).
3. Pulmonary AV fistula (a continuous murmur over the back, cyanosis, and clubbing in the absence of cardiomegaly).
4. Venous hum (an innocent condition that disappears when the patient is supine).
5. Murmurs of collaterals in patients with COA or TOF (audible in the intercostal spaces).

6. VSD + AR (maximally audible at the MLSB or LLSB, it is actually a to-and-fro murmur, rather than a continuous murmur).
7. Absence of pulmonary valve (a to-and-fro murmur, or “sawing-wood sound” at the ULSB, large central pulmonary arteries on chest radiographs, RVH on ECG, and cyanosis).
8. Aortopulmonary septal defect (AP window) (bounding peripheral pulses, a murmur resembling that of VSD, and signs of CHF).
9. Peripheral PA stenosis (a continuous murmur may be audible all over the thorax, unilateral or bilateral).
10. Ruptured sinus of Valsalva aneurysm (sudden onset of chest pain and severe heart failure, a continuous murmur or a to-and-fro murmur, and often Marfan features).

IV. PATENT DUCTUS ARTERIOSUS IN PRETERM NEONATES

A. Prevalence

Clinical evidence of PDA appears in 45% of infants <1750 g birth weight (with CHF occurring in 15%) and in about 80% of infants <1200 g birth weight (with CHF occurring in 40% to 50%).

B. Pathology and Pathophysiology

1. PDA is a special problem in premature infants with hyaline membrane disease. With improvement in oxygenation, the PVR falls rapidly, but the ductus remains patent because its responsiveness to oxygen is immature in premature newborns. The resulting large L-R shunt makes the lung stiff, and weaning the infant from the ventilator and oxygen therapy becomes difficult.
2. If the ductus is not closed, the infant remains on ventilator therapy, with development of bronchopulmonary dysplasia and pulmonary hypertension with right-sided heart failure.

C. Clinical Manifestations

1. It is important to predict a significant PDA in a premature neonate, in whom weaning from a ventilator is delayed or fails. Episodes of apnea or bradycardia may be the initial sign of PDA in infants who are not on ventilators.
2. The physical examination reveals bounding peripheral pulses, a hyperactive precordium, and tachycardia with or without gallop rhythm. The classic continuous murmur at the left infraclavicular area or ULSB is diagnostic, but the murmur may be only systolic and is difficult to hear in infants who are on ventilators.
3. The ECG is usually normal but occasionally shows LVH.
4. Chest radiographs show cardiomegaly and increased PVM in larger premature infants who are not intubated. In infants who are intubated and on high ventilator settings, chest radiographs may show the heart to be either of normal size or only mildly enlarged.
5. Two-dimensional echo and color flow Doppler studies (with the sample volume placed at the pulmonary end of the ductus) provide accurate

anatomic and functional information, such as ductal shunt patterns (pure left-to-right, bidirectional, or predominant right-to-left shunt), pressures in the PA, and magnitude of the ductal shunt or pulmonary perfusion status.

D. Management

For symptomatic infants, either pharmacologic or surgical closure of the ductus is indicated. A small PDA that does not cause symptoms should be followed medically for 6 months because of the possibility of spontaneous closure.

Medical

1. Fluid restriction to 120 mL/kg per day and a diuretic (e.g., furosemide, 1 mg/kg, 2 to 3 times a day) may be tried for 24 to 48 hours, but these regimens have a low success rate.
2. Pharmacologic closure of the PDA can be achieved with intravenous administration of indomethacin, every 12 hours, for a total of 3 doses. One example of the dosage regimen is as follows.
 - a. For <48 hours old, 0.2 mg/kg is followed by 0.1 mg/kg times 2.
 - b. For 2-7 days old, 0.2 mg/kg times 3, and
 - c. For >7 days, 0.2 mg/kg followed by 0.25 mg/kg times 2. A second course of indomethacin treatment is occasionally necessary to achieve adequate ductal closure.
3. Contraindications to the use of indomethacin include high blood urea nitrogen (>25 mg/dL) or creatinine (>1.8 mg/dL) levels, low platelet count (<80,000/mm³), bleeding tendency (including intracranial hemorrhage), necrotizing enterocolitis, and hyperbilirubinemia.
4. Alternatively, intravenous ibuprofen (10 mg/kg, followed at 24-hour intervals by two doses of 5 mg/kg) can be used, which is popular in Europe. Ibuprofen appears to have a significantly lower incidence of oliguria and a less deleterious effect on cerebral blood flow.

Surgical

If medical treatment is unsuccessful or if the use of indomethacin is contraindicated, surgical ligation of the ductus is indicated. Many centers now perform PDA ligation in the neonatal intensive care unit at the bedside. The operative mortality is 0% to 3%. The use of minimally invasive video-assisted thoracoscopic surgery (VATS) is popular in the management of PDA in low-birth-weight infants.

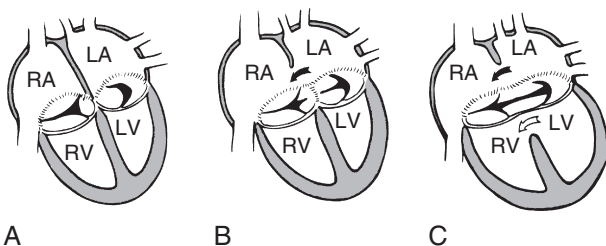
V. COMPLETE ENDOCARDIAL CUSHION DEFECT (ECD) (COMPLETE AV CANAL)

A. Prevalence

2% of all CHD. 30% of the defects occur in children with Down syndrome.

B. Pathology and Pathophysiology

1. Complete ECD consists of an ostium primum ASD, an inlet VSD, and clefts in the anterior mitral valve leaflet and in the septal leaflet of the

**FIGURE 7-9**

AV valve and cardiac septa in partial and complete ECDs. **A**, Normal AV valve anatomy with no septal defects. **B**, Partial ECD with clefts in the mitral and tricuspid valves and an ostium primum ASD (*arrow*). **C**, Complete ECD. There is a common AV valve with large anterior and posterior bridging leaflets. An ostium primum ASD (*solid arrow*) and an inlet VSD (*open arrow*) are present. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

tricuspid valve, forming common anterior and posterior cusps of the AV valve (Fig. 7-9, C). When the ventricular septum is intact, the defect is termed partial ECD or ostium primum ASD.

2. In complete ECD, a single valve orifice connects the atrial and ventricular chambers, whereas in the partial form, there are separate mitral and tricuspid orifices.
3. In the majority of complete ECD, the AV valve orifice is equally committed to the RV and LV. In some patients, however, the orifice is committed primarily to one ventricle, with hypoplasia of the other ventricle (i.e., “unbalanced” AV canal with RV or LV dominance). Hypoplasia of one ventricle may necessitate one ventricular repair (Fontan type operation).
4. Additional cardiac anomalies may include TOF (called “canal tet,” occurring in 6% of patients with ECD), DORV with more than 50% overriding of the aorta (occurring in 6%), and TGA (occurring in 3%). Associated defects are rare in children with Down syndrome.
5. The combination of these defects may result in an interatrial and/or interventricular shunt, AV valve regurgitation, or LV-to-RA shunt. CHF with or without pulmonary hypertension usually develops early in infancy.

C. Clinical Manifestations

1. Failure to thrive, repeated respiratory infections, and signs of CHF are common during early infancy.
2. Hyperactive precordium with a systolic thrill at the LLSB and a loud S2 are frequent findings. A grade 3 to 4/6 holosystolic regurgitant murmur is audible along the LLSB. The systolic murmur of MR may be audible at the apex. A mid-diastolic rumble at the LLSB or at the apex (from

relative stenosis of the tricuspid and/or mitral valve) and gallop rhythm may be present.

3. The ECG finding of a “superior” QRS axis (with the axis between -40 degrees and -150 degrees) is characteristic. RVH or RBBB is present in all, and many have LVH as well. Most patients have a prolonged PR interval (first-degree AV block).
4. Chest radiographs always show cardiomegaly with increased PVMs.
5. Two-dimensional echo and color flow Doppler studies allow imaging of all components of ECD, as well as an assessment of the hemodynamic severity.
6. CHF occurs 1 to 2 months after birth, and recurrent pneumonia is commonly seen. Children with Down syndrome and ECD begin to develop PVOD in infancy. The survivors develop PVOD and die in late childhood or as young adults.

D. Management

Medical

Medical management is recommended initially for small infants with CHF, as surgical mortality is relatively high in this age group.

Surgical

1. PA banding is no longer recommended unless other associated anomalies make complete repair a high-risk procedure. The mortality rate for PA banding is as high as 15%.
2. Closure of ASD and VSD and reconstruction of cleft AV valves under cardiopulmonary bypass and/or deep hypothermia are carried out between 2 and 4 months of age. Surgical mortality is 3% to 10%. Most of these infants have CHF that is unresponsive to medical therapy, and some have elevated PVR. Early surgical repair of the defect is especially important for infants with Down syndrome because of their known tendency to develop early PVOD. Complications of the surgery include MR (which is persistent or has been worsened), sinus node dysfunction (with resulting bradyarrhythmias), and complete heart block (occurring in less than 5% of the patients).
3. Patients with unbalanced AV canal (with hypoplasia of right or left ventricle) may be treated by an earlier PA banding and later by a modified Fontan operation.
4. In patients with “canal tet” who are severely cyanotic, a systemic-to-PA shunt is carried out during infancy and a complete repair done between 2 and 4 years of age.

Follow-Up

For patients with a significant regurgitation of the AV valve or residual ventricular shunts, anticongestive medications (e.g., diuretics, captopril, digoxin, etc.) may be required. Some restriction of activities may be required if residual hemodynamic abnormalities are present.

V. PARTIAL ENDOCARDIAL CUSHION DEFECT (OSTIUM PRIMUM ASD)**A. Prevalence**

1% to 2% of all CHD (much lower than secundum ASD).

B. Pathology and Pathophysiology

1. A defect is present in the lower part of the atrium septum near the AV valves, without an interventricular communication (see [Fig. 7-9, B](#)). The anterior and posterior bridging leaflets are fused by a connecting tongue to form separate right and left AV orifices. Clefts of the mitral and occasionally of the tricuspid valve are present.
2. Less common forms of partial ECD include common atrium (which is a characteristic lesion seen in the Ellis-van Creveld syndrome), VSD of the inlet septum (i.e., AV canal-type VSD), and isolated cleft of the mitral valve.
3. Pathophysiology of ostium primum ASD is similar to that of ostium secundum ASD.

C. Clinical Manifestations

1. Usually asymptomatic during childhood.
2. Physical findings are identical to those of secundum ASD (see [Fig. 7-2](#)), except for a regurgitant systolic murmur of MR, which may be present at the apex.
3. The ECG shows a “superior” QRS axis, as in complete ECD. First-degree AV blocks (50%) and RVH or RBBB (rsR' pattern in V1) are common.
4. Chest radiographs are identical to those of secundum ASD except for the enlargement of the LA and LV when MR is significant.
5. Two-dimensional echo allows accurate diagnosis of primum ASD.
6. CHF may develop in childhood and pulmonary hypertension in adulthood. Spontaneous closure of the defect does not occur. Cardiac arrhythmias (20%) may complicate the defect.

D. Management*Medical*

No exercise restriction is required in asymptomatic children. Occasionally, anticongestive measures with diuretic may be indicated.

Surgical

Closure of the primum ASD and reconstruction of the cleft mitral and tricuspid valves are performed electively between 2 and 4 years of age. Surgical mortality is approximately 3%.

Follow-Up

Sinus node dysfunction may develop and require pacemaker therapy.

VI. PARTIAL ANOMALOUS PULMONARY VENOUS RETURN**A. Prevalence**

Less than 1% of all children with CHD.

B. Pathology and Pathophysiology

1. One or more but not all pulmonary veins (PVs) drain into the RA or its venous tributaries such as the SVC, IVC, coronary sinus, or left innominate vein.
2. The right PVs are involved twice as often as the left PVs. The right PVs may drain into the SVC, often associated with sinus venous ASD, or drain into the IVC in association with an intact atrial septum and bronchopulmonary sequestration. The left PVs drain either into the left innominate vein or into the coronary sinus.
3. The hemodynamic alteration is similar to that seen with ASD. The magnitude of the pulmonary blood flow is determined by the number of anomalous PVs and the presence and size of the ASD.

C. Clinical Manifestations

1. Children with PAPVR are usually asymptomatic.
2. Physical findings are similar to those of ASD (see Fig. 7-2). When associated with ASD, the S2 is split widely and fixed. When the atrial septum is intact, the S2 is normal.
3. The ECG shows RVH or RBBB or is normal.
4. Chest radiographs show RAE, RVE, and increased PVMs.
5. Echo diagnosis of PAPVR is less reliable. Cardiac MRI can make correct diagnosis of the condition without catheterization.
6. If PAPVR is undetected, cyanosis and exertional dyspnea may develop during the third and fourth decades, resulting from pulmonary hypertension and PVOD.

D. Management

Medical

Exercise restriction is not required.

Surgical

1. Surgical correction is carried out when the patient is 2 to 5 years of age. A significant L-R shunt with Qp/Qs greater than 1.5:1 or 2:1 is an indication for surgery. Isolated single lobe anomaly is not ordinarily corrected.
2. Surgical procedures vary according to the site of anomalous drainage.
 - a. For the anomalous drainage into the SVC, a tunnel is created between the anomalous vein and the ASD using a Teflon or pericardial patch and the SVC is widened to prevent obstruction of flow.
 - b. For the anomalous drainage into the IVC, an intraatrial tunnel drains the venous blood into the LA. When this is associated with the bronchopulmonary sequestration, the involved lobes(s) may be resected (without connecting the anomalous vein to the heart).
 - c. When the left PVs drain into the coronary sinus, the sinus is unroofed and the orifice of the coronary sinus is closed.

Chapter 8

Obstructive Lesions

I. PULMONARY STENOSIS

Prevalence

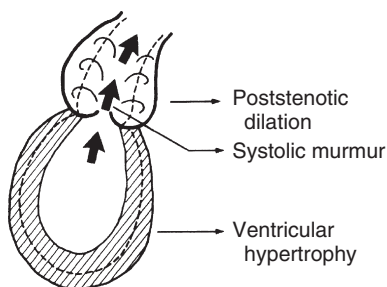
5% to 8% of children with CHDs.

Pathology and Pathophysiology

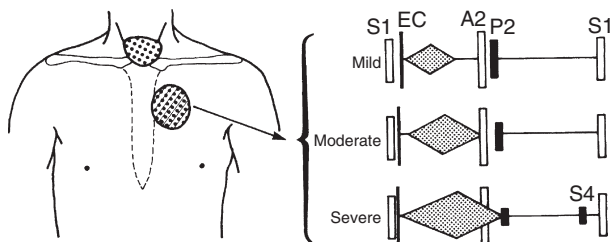
1. PS may be valvular (90%), subvalvular (infundibular), or supravulvular (i.e., stenosis of the main PA). Stenosis of the PA branches is presented in Chapter 10.
 - a. In valvular PS, the pulmonary valve is thickened, with fused or absent commissures and a small orifice. A poststenotic dilatation of the MPA usually develops with valvular PS.
 - b. Dysplastic pulmonary valve (with thickened, irregular, immobile tissue) is frequently seen with Noonan syndrome.
 - c. Infundibular PS is usually associated with a large VSD as seen in TOF. The poststenotic dilatation is not seen with subvalvular stenosis.
2. In so-called double-chambered RV, abnormal muscular bands (running between the ventricular septum and the anterior wall) divide the RV cavity into a proximal high-pressure chamber and a distal low-pressure chamber.
3. Depending on the severity of PS, a varying degree of RVH develops. The RV is usually normal in size, but in newborns with critical PS, the RV is hypoplastic.
4. In general, three pathophysiologic changes occur in obstructive lesions such as PS (or AS). They are (1) systolic ejection murmur on auscultation, (2) hypertrophy of the responsible ventricle, and (3) poststenotic dilatation (Fig. 8-1).

Clinical Manifestations

1. Usually asymptomatic with mild PS. Exertional dyspnea and easy fatigability may be seen in moderately severe cases, and CHF occurs in severe cases. Neonates with critical PS are cyanotic and tachypneic.
2. An ejection click is present at the ULNB with valvular PS (Fig. 8-2). The S2 may split widely, and the P2 may be diminished in intensity. A systolic ejection murmur (grade 2 to 5/6) with or without systolic thrill is best audible at the ULNB and transmits fairly well to the back and axillae. The louder and longer the murmur, the more severe is the stenosis. Neonates with critical PS may have only a faint heart murmur, if any.
3. The ECG is normal in mild PS. RAD and RVH are present in moderate PS. RAH and RVH with “strain” pattern are present in severe PS.

**FIGURE 8-1**

Three secondary changes seen in ventricular outflow obstructive lesions, such as pulmonary stenosis or aortic valve stenosis.

**FIGURE 8-2**

Cardiac findings of pulmonary valve stenosis. Abnormal sounds are shown in *black*. Dots represent areas with systolic thrill. EC, Ejection click.

Neonates with critical PS may show LVH (due to hypoplastic RV and relatively large LV).

4. Chest radiographs show normal heart size and a prominent MPA segment (i.e., poststenotic dilatation). PVMs are normal but may be decreased in severe PS.
5. Two-dimensional echo and Doppler echo studies:
 - a. Thickened pulmonary valve with restricted systolic motion (doming) and a poststenotic dilatation of the MPA are commonly seen.
 - b. The severity of PS (by peak Doppler pressure gradient) may be classified as follows
 - (1) Mild: <35 to 40 mm Hg (or RV pressure <50% of LV pressure).
 - (2) Moderate: gradient 40 to 70 mm Hg (or RV pressure 50% to 75% of LV pressure).
 - (3) Severe: >70 mm Hg (or RV pressure \geq 75% of LV pressure).
6. The severity of the obstruction is usually not progressive in mild PS, but it tends to progress with age in moderate or severe PS. CHF may

develop in patients with severe stenosis. Sudden death is possible in patients with severe stenosis during heavy physical activities.

Management

Medical

1. For neonates with critical PS and cyanosis, prostaglandin E₁ (PGE₁) infusion should be started to reopen the ductus. Balloon valvuloplasty is the procedure of choice in critically ill neonates. Even dysplastic valves appear to mature after the procedure. Some patients require reintervention (either repeat valvuloplasty or surgery) at a later time.
2. Balloon valvuloplasty is the procedure of choice for significant pulmonary valve stenosis. Cardiac catheterization is recommended for the balloon procedure in patients with a Doppler pressure gradient near 50 mm Hg. Indications for the balloon procedure may include the following.
 - a. Pressure gradient >40 mm Hg with the patient sedated in the catheterization laboratory.
 - b. If the catheterization pressure gradient is 30 to 39 mm Hg, the balloon procedure is reasonable.
 - c. Symptoms (angina, syncope, or pre-syncope) attributable to PS with catheter gradient >30 mm Hg.
 - d. It is reasonable to try on dysplastic pulmonary valve (with lower success rate of 65%).
3. Complications of the balloon procedure.
 - a. PR is common after balloon dilatation (occurring in 10% to 40%). Therefore, use of a balloon 120% to 140% of the pulmonary annulus is now recommended to reduce the incidence of PR.
 - b. Following relief of severe PS, hypertrophied dynamic infundibulum may cause a persistent pressure gradient, with rare occurrence of fatal outcome ("suicidal right ventricle"). Propranolol may be given to reduce the hyperdynamic response.
4. Restriction of activity is usually not indicated except for severe PS.

Surgical

1. Surgical valvotomy is occasionally indicated in patients with valvular PS in whom balloon valvuloplasty is unsuccessful.
2. Surgery is indicated in patients with dysplastic pulmonary valves which are resistant to dilatation. Dysplastic valve may need to be completely excised because simple valvotomy may be ineffective.
3. Surgery is also indicated for infundibular stenosis and anomalous RV muscle bundle with significant pressure gradients.
4. If balloon valvuloplasty is unsuccessful, infants with critical PS require surgery on an urgent basis.
5. Stenosis at the main PA requires patch widening of the narrow portion.

Follow-Up

Periodic echo studies are indicated to detect recurrences or worsening of the stenosis.

II. AORTIC STENOSIS

Prevalence

A group of lesions that produce LV outflow tract obstruction account for 10% of all CHD. Aortic valve stenosis occurs more often in males (male-female ratio of 4:1).

Pathology and Pathophysiology

1. LVOT obstruction may occur at the valvular, subvalvular, or supravalvular levels (Fig. 8-3).
2. Valvular AS is caused most often by a bicuspid aortic valve (with a fused commissure), and less commonly by a unicuspid valve (with one lateral attachment) or stenosis of the tricuspid (tricommissural) valve (Fig. 8-4). Many cases of bicuspid aortic valve are nonobstructive during childhood.
3. Symptomatic neonates with so-called critical neonatal aortic valve stenosis have primitive, myxomatous valve tissue, with a pinhole opening. The aortic valve ring and ascending aorta, the mitral valve, and the LV cavity are almost always hypoplastic (often requiring Norwood operation followed by Fontan operation).
4. Supravalvular AS occurs at the upper margin of the sinus of Valsalva. This is often associated with Williams syndrome.
5. Subvalvular (subaortic) stenosis may be either discrete (simple membrane or fibromuscular ridge) or diffuse tunnel-like fibromuscular narrowing (tunnel stenosis).
 - a. Discrete subaortic stenosis is more common than the tunnel stenosis and is often associated with other lesions such as VSD, PDA, or COA. Occasionally, its development follows surgical interventions, such as closure of VSD or PA banding.

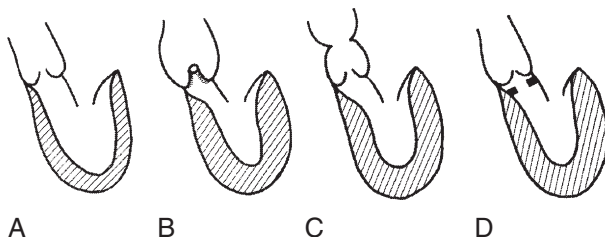


FIGURE 8-3

Anatomic types of LV outflow tract obstruction. **A**, Normal. **B**, Valvular stenosis. **C**, Supravalvular stenosis. **D**, Discrete subaortic stenosis. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, 2014, Mosby.)

- b. Tunnel-like subaortic stenosis is often associated with hypoplasia of the valve ring and the ascending aorta. It may be a part of Shone complex (comprising supramitral ring, parachute mitral valve, subaortic stenosis, and COA).
6. Hypertrophy of the LV may develop if the stenosis is severe. A post-stenotic dilatation of the ascending aorta is present in valvular AS. AR usually develops with subaortic AS.

Clinical Manifestations

1. Patients with mild to moderate AS are asymptomatic. Exertional chest pain or syncope may occur with severe AS. CHF develops within the first few months of life with critical AS.
2. Blood pressure is normal in most patients, but a narrow pulse pressure is present in severe AS. Patients with supravalvular AS may have a higher systolic pressure in the right arm than in the left (due to the jet of stenosis directed into the innominate artery, the so-called Coanda effect).
3. A systolic thrill may be present at the URSB, in the suprasternal notch, or over the carotid arteries. An ejection click may be audible with valvular AS. A harsh systolic ejection murmur (grade 2 to 4/6) is best audible at the 2RICS or 3LICS (Fig. 8-5), with good transmission to the neck and frequently to the apex. A high-pitched, early diastolic decrescendo murmur of AR may be audible in patients with bicuspid aortic valve and

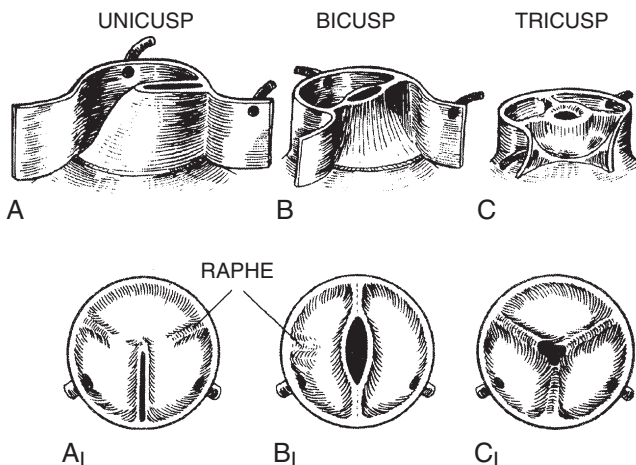
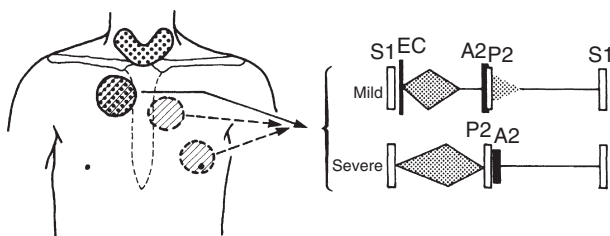


FIGURE 8-4

Anatomic types of aortic valve stenosis. Top row is the side view, and bottom row is the view as seen in surgery during aortotomy. **A**, Unicuspid aortic valve. **B**, Bicuspid aortic valve. **C**, Stenosis of a tricuspid aortic valve. (From Goor DA, Lillehei CW: *Congenital Malformations of the Heart*. New York, 1975, Grune & Stratton.)

**FIGURE 8-5**

Cardiac findings of aortic valve stenosis. Abnormal sounds are indicated in *black*. Systolic thrill may be present in areas with *dots*. EC, Ejection click.

those with discrete subvalvular stenosis. In symptomatic infants with critical AS, the heart murmur may be absent or faint, and the peripheral pulses are weak and thready.

4. The ECG is normal in mild cases. LVH with or without a strain pattern is seen in more severe cases.
5. Chest radiographs are usually normal in children, but a dilated ascending aorta may be seen occasionally in valvular AS. A significant cardiomegaly develops with CHF or substantial AR.
6. Echo and Doppler studies are diagnostic.
 - a. Two-dimensional echo shows the anatomy of the aortic valve (bicuspid, tricuspid, or unicuspid) and that of subvalvular and supra-aortic AS.
 - b. The Doppler pressure gradient is best obtained in the apical “five-chamber” view. The Doppler pressure gradient (instantaneous gradient) is approximately 20% higher than the peak-to-peak systolic pressure gradient obtained during cardiac catheterization.
 - c. The severity of AS by Doppler peak (and mean) gradients and by peak-to-peak catheter gradient may be classified as follows.
 - (1) Mild: A peak Doppler gradient <40 mm Hg (mean Doppler <25 mm Hg [or peak-to-peak gradient <30 mm Hg])
 - (2) Moderate: A peak Doppler gradient 40 to 70 mm Hg (mean Doppler 25 to 40 mm Hg [or peak-to-peak gradient 30 to 50 mm Hg])
 - (3) Severe: A peak Doppler gradient >70 mm Hg (mean Doppler >40 mm Hg [or peak-to-peak gradient >50 mm Hg])
 - d. For the discrete membranous stenosis, one should note (1) the length of the membrane, (2) the pressure gradient across the obstruction, (3) the distance of the membrane from the aortic valve, (4) the extension of the membrane onto the aortic or mitral valve, (5) the presence of aortic regurgitation, and (6) associated cardiac lesions. Some of these have been linked to the risk of recurrence requiring surgery (see below).
7. Natural history.

Mild stenosis frequently becomes more severe with time. The stenosis may worsen with aging as the result of calcification of the valve cusps

(requiring valve replacement surgery in some adult patients).
Progressive AR is possible in discrete subaortic stenosis.

Management

Medical

1. In critically ill neonates and infants with CHF, anticongestive measures with fast-acting inotropic agents and diuretics, with or without PGE₁ infusion, are indicated, in preparation for either balloon valvuloplasty or surgery.
2. Serial echo Doppler studies are needed every 1 to 2 years because AS of all severities tends to worsen with time.
3. Percutaneous balloon valvuloplasty:
 - a. Balloon procedure is now regarded as the first step in management of symptomatic neonates in many centers. Although the results are promising, they are not as good as those for PS. A survival rate of 50% has been reported in neonates. Serious complications (major hemorrhage, loss of femoral artery pulse, avulsion of part of the aortic valve leaflet, perforation of the mitral valve or LV) can occur.
 - b. It is also the first interventional method for children older than 1 year of age with aortic valve stenosis. For subaortic stenosis, the balloon procedure is not effective.
 - c. The following may be indications for the procedure (AHA, 2011).
 - (1) Newborns with isolated critical valvular AS who are ductal dependent.
 - (2) Children with isolated valvular AS who have depressed LV systolic function.
 - (3) Children with isolated valvular AS who have a peak-to-peak systolic gradient of ≥ 50 mm Hg by cardiac catheterization.
 - (4) Children with isolated valvular AS who have a peak systolic gradient ≥ 40 mm Hg, if there are symptoms of angina or syncope or ischemic ST-T wave changes on the ECG at rest or with exercise.
4. Activity restrictions.
 - a. No limitation in activity is required for mild AS.
 - b. For patients with moderate AS, varying levels of activity restriction are required as suggested below.
 - c. Patients with severe AS should not participate in any competitive sports.

Surgical

1. For valvular AS:
 - a. Indications:
 - (1) Failed balloon valvuloplasty or severe AR resulting from the procedure.
 - (2) A sick newborn with critical AS, who had failed balloon valvuloplasty.
 - b. Procedures: Either (1) aortic valve commissurotomy, (2) aortic valve replacement (using mechanical or biological valves), or (3) the Ross procedure (preferred, see below) is performed. The advantage of the mechanical valve is durability, but it has the tendency for thrombus

formation with a potential embolization, requiring anticoagulation with warfarin with its attendant risks of bleeding and its known teratogenic effects. Biological valves do not require anticoagulation with warfarin but the deterioration occurs within a decade or two, due to degeneration and calcification. Homografts are preferred for adolescent girls or women in child-bearing age because anticoagulation with warfarin is not required.

- c. In the **Ross procedure** (or pulmonary root autografts), the autologous pulmonary valve replaces the aortic valve, and an aortic or a pulmonary allograft replaces the pulmonary valve (Fig. 8-6). The pulmonary valve autograft has the advantage of documented long-term durability; it does not require anticoagulation and there is evidence of the autograft's growth. The patient's own aortic valve may be used for pulmonary position after aortic valvotomy ("double" Ross procedure).
2. For discrete subaortic stenosis:
 - a. Indications: Peak gradient >35 mm Hg and at least mild AR are the most commonly accepted indications. Occasionally, the presence of one of them may be an indication for intervention. Most centers accept the onset of AR as an indication for surgical removal of the membrane.
 - b. Procedures: Excision of the membrane is done.
 - c. A tendency for recurrence after surgical excision of subaortic membrane has been a concern, with a recurrence rate as high as 25% to 30%. Risk factors for recurrence include (a) younger age (<4 year),

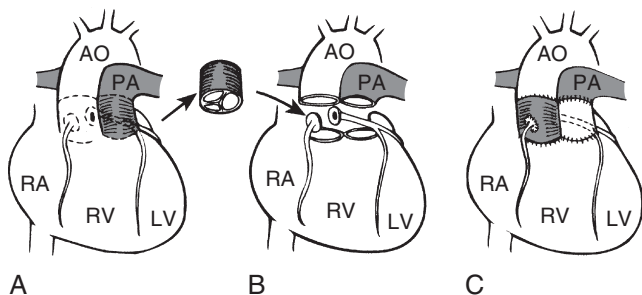


FIGURE 8-6

Ross procedure (or pulmonary root autograft). **A**, The two horizontal lines on the aorta (AO) and pulmonary artery (PA) and two broken circles around the coronary artery ostia are lines of proposed incision. The pulmonary valve, with a small rim of right ventricular (RV) muscle, and the adjacent PA are removed. **B**, The aortic valve and the adjacent aorta have been removed, leaving buttons of aortic tissue around the coronary arteries. **C**, The pulmonary autograft is sutured to the aortic annulus and to the distal aorta, and the coronary arteries are sutured to openings made in the PA. The pulmonary valve is replaced with either an aortic or a pulmonary allograft. LV, left ventricle; RA, right atrium. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

(b) high pressure gradient (>50 mm Hg), (c) proximity of the membrane to the aortic valve (<6 mm), and (d) extension of the membrane to the aortic or mitral valves. Some centers delay surgery until after 10 years of age because the recurrence is very rare after this age. More aggressive resection of the membrane and extensive myectomy reduced the recurrence but resulted in a higher complication rate of heart block (14%). Surgical mortality for subaortic membrane is near zero.

- d. Patients with the following are considered low risk, and medical follow-up, rather than surgical intervention, is recommended: Those with (a) no or trace AR, (b) Doppler gradient ≤ 30 mm Hg, (c) the membrane not in proximity to the aortic valve (>6 mm), and (d) thin and mobile aortic valve.
3. **For tunnel-type subaortic stenosis**, a pressure gradient ≥ 50 mm Hg is an indication for surgery. Valve replacement following aortic root enlargement (Kono procedure) may be performed.
4. **For supralvalvar AS**, peak pressure gradient >50 to 60 mm Hg, severe LVH, or appearance of new AR is an indication for surgery. Widening of the stenotic area using a diamond-shaped fabric patch may be performed.

Follow-Up

1. Annual follow-up is required for all patients who had a balloon or surgical procedure done for the aortic valve because significant AR develops in 10% to 30% of the patients and the discrete subaortic membrane recurs in 25% to 30% after surgical resection.
2. Anticoagulation with warfarin is needed after a prosthetic mechanical valve replacement. The INR should be maintained between 2.5 and 3.5 for the first 3 months and between 2.0 and 3.0 beyond that time. Low-dose aspirin (81 mg per day) is also indicated in addition to warfarin.
3. After aortic valve replacement with bioprosthesis, aspirin (81 mg) is indicated (without warfarin).
4. SBE prophylaxis is required after placement of prosthetic material or valve, when indications arise.
5. Restriction from competitive sports may be necessary for children with moderate residual AS and/or AR.

III. COARCTATION OF THE AORTA

Prevalence

8% to 10% of CHD, with a male preponderance (2:1). Among patients with Turner syndrome, 30% have COA.

Pathology and Pathophysiology

1. Narrowing of the upper thoracic aorta is present, most commonly distal to the left subclavian artery.
2. There are two groups of patients with COA: symptomatic infants and asymptomatic children.

- a. In *symptomatic infants* with COA, other cardiac defects (such as aortic hypoplasia, VSD, PDA, and mitral valve anomalies) are often present. These abnormalities may have reduced antegrade flow through the aorta during fetal life and may have caused a poor development of collateral circulation around the COA.
- b. In *asymptomatic children* with COA, associated anomalies are uncommon.
3. COA may occur in association with other CHDs, such as TGA and DORV (e.g., Taussig-Bing abnormality).
4. As many as 85% of patients with COA have a bicuspid aortic valve.

Clinical manifestations and management of the two groups are quite different; therefore they will be presented under separate headings.

A. SYMPTOMATIC INFANTS

Clinical Manifestations

1. Signs of CHF (poor feeding, dyspnea) and renal failure (oliguria, anuria) with general circulatory shock may develop in the first 2 to 6 weeks of life.
2. A loud gallop and weak and thready pulses, without heart murmur, are common findings in sick infants.
3. The ECG usually shows RVH or RBBB, rather than LVH.
4. Chest radiographs show a marked cardiomegaly and signs of pulmonary edema or pulmonary venous congestion.
5. Two-dimensional echo shows the site and extent of the COA and other associated cardiac defects.
 - a. In the suprasternal notch view, a thin wedge-shaped “posterior shelf” is imaged distal to the left subclavian artery. Varying degrees of isthmus hypoplasia and hypoplasia of the transverse aortic arch may be present. Poststenotic dilatation of the descending aorta is usually imaged.
 - b. Other associated defects such as bicuspid aortic valve and VSD can be imaged.
 - c. Delayed rate of systolic upstroke and persistent diastolic flow in the abdominal aorta may suggest the diagnosis.
 - d. Diagnosis of neonatal COA in the presence of PDA is difficult. The aortic isthmus ≤ 3 mm without PDA or the isthmus ≤ 4 mm in the presence of PDA may be diagnostic of neonatal COA. The ratio of the aortic isthmus to the descending aorta at the diaphragm < 0.64 is also a reliable sign of COA in the presence of PDA.
 - e. Doppler studies above and below the coarctation site should be obtained in assessing the severity of the coarctation.
6. MRI has become the imaging modality of choice after echo diagnosis of the condition, rather than cardiac catheterization (before interventional treatment).
7. Early death from CHF and renal failure is possible.

Management

Medical

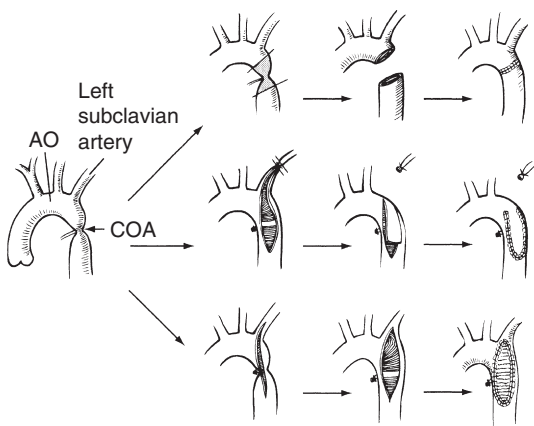
1. Intensive anticongestive treatment should be given with fast-acting inotropic agents (catechols), diuretics, and oxygen to stabilize the patient.
2. PGE₁ infusion is indicated to reopen the ductus before any surgical repair or balloon procedure takes place (see Appendix E for the dosage of PGE₁).
3. Balloon angioplasty with or without stent implantation is controversial but it has emerged as a less invasive alternative to surgery for sick infants. Some centers use cutting balloons or a low-profile stent in very sick infants, which does not require overexpansion of the coarctation segment and thus is less likely to produce aneurysm. When a stent is used, it is usually not expandable to adult size and requires surgical removal at a later date.
4. Balloon angioplasty is associated with a higher rate of recoarctation (>50%) than surgical repair, and the rate of complications (including femoral artery injury) is high during infancy.

Surgical

1. If CHF develops, the need for surgery or nonsurgical intervention is urgent. Surgical procedure of choice varies from institution to institution.
 - a. Extended resection with an end-to-end anastomosis (preferable when possible), subclavian flap aortoplasty, or patch angioplasty is performed (Fig. 8-7).
 - b. The mortality rate for isolated COA is less than 5%. Postoperative renal failure is the most common cause of death. Residual obstruction and/or recoarctation occur in up to one third of all cases, but the recurrence rate appears lower than that following balloon angioplasty.
2. If it is associated with a VSD, one of the following procedures may be performed.
 - a. If the VSD appears restrictive, COA repair only without PA banding is done. If CHF persists, VSD closure is indicated.
 - b. If the PA pressure remains high after completing the COA repair, PA banding may be performed. Later VSD repair and removal of the PA band are done when the patient is 6 to 24 months of age.
 - c. If the VSD appears nonrestrictive, repairing COA and VSD at the same operative setting is preferred by many centers.

Follow-Up

1. Reexamination every 6 to 12 months is indicated, since recoarctation is possible, especially when surgery is performed in the first year of life.
2. Balloon angioplasty may be performed if a significant recoarctation develops.
3. Surveillance for and treatment of systemic hypertension is needed.

**FIGURE 8-7**

Surgical techniques for repair of COA. *Top*, End-to-end anastomosis. *Middle*, Subclavian flap procedure. *Bottom*, Patch aortoplasty. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

B. ASYMPTOMATIC CHILDREN

Clinical Manifestations

1. These children are usually asymptomatic except for rare complaints of leg pain.
2. The pulse in the leg is absent or weak and delayed. Hypertension in the arm or higher BP readings in the arm than the thigh may be present. An ejection click resulting from the bicuspid aortic valve is frequently audible at the apex and/or base. A systolic ejection murmur, grade 2 to 3/6, is audible at the URSB and MLSB and in the left interscapular area in the back.
3. The ECG usually shows LVH, but it may be normal.
4. Chest radiographs show a normal or slightly enlarged heart. A "3 sign" on overpenetrated films or an "E sign" on the barium-filled esophagus may be present. Rib notching may be seen in children after about 5 years of age.
5. Two-dimensional echo studies:
 - a. A discrete, shelf-like membrane in the posterolateral aspect of the descending aorta is imaged.
 - b. Doppler examination reveals disturbed flow and increased flow velocity distal to the COA.
 - c. Continuous wave Doppler flow profile distal to the coarctation is composed of two superimposed signals representing the proximal and distal flows.

- d. The flow velocities proximal and distal to the coarctation site should be used in estimating pressure gradients. This is because the proximal flow velocity is often higher than 1.5 m/sec and it cannot be ignored in the Bernoulli equation.
- e. In severe COA with extensive collaterals, the Doppler-estimated gradient may underestimate the severity of the coarctation.
- f. The bicuspid aortic valve is frequently imaged.
6. MRI with 3D reconstruction, supplemented by gadolinium contrast, has become the imaging modality of choice. Cardiac catheterization is no longer needed for anatomic assessment.
7. The bicuspid aortic valve may cause stenosis and/or regurgitation later in life. If a COA is left untreated, LV failure, intracranial hemorrhage, or hypertensive encephalopathy may develop later in life.

Management

Medical

1. Hypertension or hypertensive crisis should be detected and treated. Arm and leg BPs should be checked for increasing pressure differences (possible recurrence). Reduced BP readings in the lower extremities may be due to femoral artery injuries resulting from previous surgeries or interventional procedures.
2. Balloon angioplasty for native (unoperated) COA is controversial.
 - a. Some centers use the balloon procedure for the native COA, while other centers prefer a surgical approach.
 - b. Indications for balloon intervention:
 - (1) Trans-catheter systolic gradient across COA of >20 mm Hg and suitable anatomy, irrespective of patients' age.
 - (2) Trans-catheter systolic gradient of <20 mm Hg with suitable angiographic anatomy (i) in the presence of significant collateral vessels, (ii) in patients with univentricular heart, or (iii) in patients with significant LV dysfunction.
 - (3) It may be reasonable to consider the procedure for native coarctation as a palliative procedure at any age when there is (i) severe LV dysfunction, (ii) severe mitral regurgitation, or (iii) systemic disease affected by the cardiac condition.
 - c. The most common acute complication of the balloon angioplasty is femoral artery injury and thrombosis, especially in small children. There is a possibility of aortic aneurysm formation with serious late complications.
3. A balloon-expandable stainless steel stent implanted concurrently with balloon angioplasty is gaining popularity. Currently the aortic stent is used for older children (at least 8 to 10 years old) and the stent used should be expandable to an adult size (minimum of 20 mm in diameter). Indications for its use are similar to those described for balloon angioplasty above. For patients in whom balloon angioplasty has failed, it is reasonable to use stent placement.

4. An absorbable metal stent is in the experimental stage. This could be used in infants and small children on whom repeat dilatation of the stent may be necessary.

Surgical

1. Indications for surgery:
 - a. Reduction of aortic diameter by 50% at the level of coarctation (determined by echo or MRI) in the presence of a pressure gradient of more than 20 to 30 mm Hg is considered an absolute indication for surgery.
 - b. Significant narrowing of the aorta with a Doppler pressure gradient >20 to 30 mm Hg is considered an indication for surgery in asymptomatic children. (The same degree of pressure gradient by arm and leg BP measurements is a less reliable indication.)
 - c. Some recommend surgery if a prominent gradient develops with exercise. This is not reliable; it may be due to peripheral amplification of systolic pressure seen in the arm as discussed in Chapter 5 (see [Fig. 5-1](#)).
2. The preferred age for surgery varies from center to center; some centers prefer 2 to 3 years of age while others prefer 4 to 5 years of age. Surgery done before 1 year of age may have lower incidence of hypertension but recurrence rate is high.
3. Resection of the coarctation segment and an end-to-end anastomosis constitute the procedure of choice. Other surgical options are illustrated in [Figure 8-7](#).

8

Follow-Up

1. Annual examination is recommended with attention to (1) BP differences in the arm and leg (recoarctation), (2) status of associated abnormalities such as bicuspid aortic valve or mitral valve disease, and (3) possible development of subaortic AS.
2. Possible late complications include aneurysm formation (with likelihood of dissection and rupture), for which MRI or CT angiography is the preferred method (performed every 2 to 5 years).

IV. INTERRUPTED AORTIC ARCH

Prevalence

1% of critically ill infants with CHDs.

Pathology and Pathophysiology

1. This extreme form of COA is divided into three types according to the location of the interruption ([Fig. 8-8](#)).
 - a. In type A, the interruption is distal to the left subclavian artery (occurring in 30% of patients).
 - b. In type B, the interruption is between the left carotid and left subclavian arteries (occurs in 43% of cases). DiGeorge syndrome occurs in about 50% of patients with type B interruption.

- c. In type C, the interruption is between the innominate and left carotid arteries (occurs in 17% of cases).
2. PDA and VSD are almost always associated with this defect. A bicuspid aortic valve (60%), mitral valve deformity (10%), persistent truncus arteriosus (10%), or subaortic stenosis (20%) may be present.
3. DiGeorge syndrome occurs in at least 15% of these patients.

Clinical Manifestations

1. Respiratory distress, cyanosis, poor peripheral pulse, or circulatory shock develops in the first few days of life.
2. Cardiac findings are nonspecific.
3. Chest radiographs show cardiomegaly, increased PVM, and pulmonary edema. The upper mediastinum may be narrow (due to the absence of thymus, i.e., DiGeorge syndrome).
4. The ECG may show RVH.
5. Echo studies are useful in the diagnosis of the condition.
6. Cardiac CT or MRI is more frequently used than angiocardiology to clarify the anatomy before surgery.

Management

Medical

1. PGE₁ infusion (see Appendix E for dosage), intubation, and oxygen administration.
2. Workup for DiGeorge syndrome (i.e., serum calcium) should be carried out.
3. Citrated blood (that causes hypocalcemia by chelation) should not be transfused. Blood should be irradiated before transfusion in patients with DiGeorge syndrome.

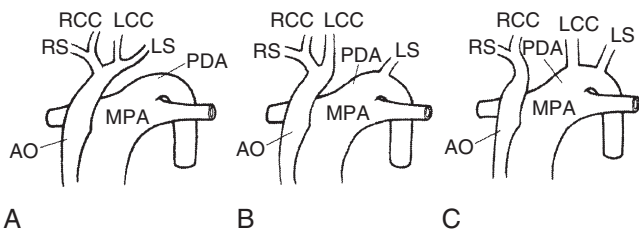


FIGURE 8-8

Three types of aortic arch interruption. **A**, Type A. **B**, Type B. **C**, Type C (see text). AO, aorta; LCC, left common carotid; LS, left subclavian; MPA, main pulmonary artery; PDA, patent ductus arteriosus; RCC, right common carotid; RS, right subclavian. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

Surgical

1. Surgical repair of the interruption (primary anastomosis, Dacron vascular graft, or venous homograft) and closure of a simple VSD are recommended if possible.
2. If associated with complex defects, repair of the interruption and PA banding are performed, with complete repair at a later time.

V. PULMONARY ARTERY STENOSIS

Prevalence

PA stenosis accounts for >3% of all CHDs.

Pathology

1. Stenosis of the PA occurs either at the main PA or in the peripheral pulmonary arteries. The most frequent site of stenosis is near the bifurcation as an isolated anomaly.
2. It is associated with other CHDs (such as valvular PS, ASD, VSD, PDA, and TOF).
3. When associated with cyanotic CHDs (such as pulmonary atresia with intact ventricular septum or TOF with pulmonary atresia), the stenosis usually involves multiple branches and multiple sites.
4. It may also be seen in other conditions such as rubella syndrome, Williams syndrome, and Allergille syndrome.
5. Some PA stenosis is secondary to surgical procedures, such as previous B-T shunt.

Clinical Manifestation

1. Mild stenosis of the PAs causes no symptoms. If the stenosis is severe and bilateral, the RV may hypertrophy.
2. An ejection systolic murmur grade 2 to 3/6 is audible at the ULNB, with good transmission to the ipsilateral axilla and back. The S2 is either normal or more obviously split.
3. The ECG is normal with mild stenosis, but it shows RVH with severe stenosis.
4. Chest radiographs usually are normal.
5. Echo and Doppler studies may show stenoses in the main PA or near the bifurcation, but those in smaller branches cannot be imaged by echo.
 - a. When unilateral PA stenosis is identified, Doppler evaluation of the severity of the stenosis becomes difficult because of abnormal flow distribution in the lungs (with discrepant blood flow away from the stenotic branch).
 - b. Many significant stenoses may not be demonstrable by pressure gradient in a low pulmonary flow situation (such as seen with Glenn shunt and Fontan circulation).
 - c. In general a significant PA stenosis is present when:
 - (1) There is a Doppler pressure gradient of >20 to 30 mm Hg,
 - (2) RV or main PA pressure is higher than 50% of systemic pressure, or

- (3) Lung perfusion scan shows relative flow discrepancy between two lungs of 35%/65% or worse, rather than the normal right/left perfusion ratio of 55/45. (Recently, the normal right/left perfusion ratio was found to be 52.5/47.5 [\pm 2.1%].)
6. Lung perfusion scan had been a useful noninvasive method in determining relative pulmonary flow. However, washout effects from additional blood supply to the lung can make flow quantification inaccurate. Currently, MRI represents the gold standard for assessing differential blood flow (better than lung perfusion scan).
7. In patients with multiple previous stenting of the pulmonary tree, contrast-enhanced CT imaging is preferred. Angiocardiology is the best invasive tool in the diagnosis of peripheral PA stenosis.

Management

1. Mild to moderate PA stenoses usually do not require treatment, but severe ones do.
2. The central (extraparenchymal) type is surgically amenable, but the peripheral (intraparenchymal) type is not correctable by surgery; catheter therapy is often the only option.
3. For peripheral PA stenosis, standard balloon angioplasty, cutting balloons, and the placement of an endovascular stent are available.
 - a. Low-pressure balloon angioplasty has a limited success rate (\approx 50%) and a high (16%) recurrence rate. High-pressure balloon (20 to 25 atm) is more effective.
 - b. A stainless steel balloon-expandable stent may offer better results.
 - c. Using a cutting balloon alone or followed by high-pressure ballooning is best suited for small, lobar pulmonary artery branches not amenable to stenting.

Cyanotic Congenital Heart Defects

I. COMPLETE TRANSPOSITION OF THE GREAT ARTERIES

Prevalence

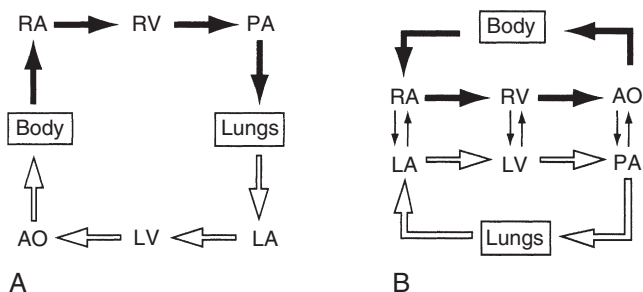
TGA constitutes 5% of all CHD. It is more common in boys (3:1).

Pathology and Pathophysiology

1. The aorta (AO) and the pulmonary artery are transposed, with the AO arising anteriorly from the RV, and the PA arising posteriorly from the LV. The end result is complete separation of the two circuits, with hypoxemic blood circulating in the body and hyperoxemic blood circulating in the pulmonary circuit (Fig. 9-1). The classic complete TGA is called *D*-transposition, in which the aorta is located anteriorly and to the *right* of the PA; hence, *D*-TGA. (When the transposed aorta lies to the *left* of the PA, it is called *L*-transposition.)
2. Defects that permit mixing of the two circulations, such as ASD, VSD, and PDA, are necessary for survival. A VSD is present in 40% of cases. In about 50% of the patients no associated defects are present other than PFO, small ASD, or small PDA.
3. LVOT obstruction (subpulmonary stenosis), either dynamic or fixed obstruction, occurs in about 5% of patients without VSD. PS occurs in 30% to 35% of patients with VSD.
4. In neonates with poor mixing of the two circulations, progressive hypoxia and acidosis result in early death, requiring an early intervention.

Clinical Manifestations

1. Cyanosis and signs of CHF develop in the newborn period. Severe arterial hypoxemia unresponsive to oxygen inhalation and acidosis are present in neonates with poor mixing. Hypoglycemia and hypocalcemia are occasionally present.
2. Auscultatory findings are nonspecific. The S2 is single and loud. No heart murmur is audible in infants with intact ventricular septum. When TGA is associated with VSD or PS, a systolic murmur of these defects may be audible.
3. The ECG shows RAD and RVH. An upright T wave in V1 after 3 days of age may be the only abnormality suggestive of RVH. BVH may be present in infants with large VSD, PDA, or PS.
4. Chest radiographs show cardiomegaly with increased PVMs. An egg-shaped cardiac silhouette with a narrow superior mediastinum is characteristic.

**FIGURE 9-1**

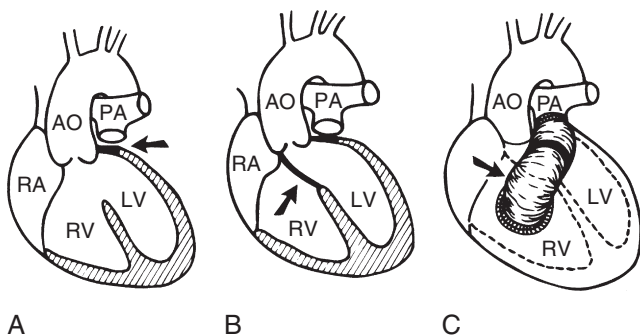
Circulation pathways of normal serial circulation (**A**) and parallel circulation of TGA (**B**). Open arrows indicate oxygenated blood, and solid arrows, desaturated blood. AO, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium, RV, right ventricle.

5. Two-dimensional echo study is diagnostic.
 - a. It fails to show a “circle-and-sausage” pattern of the normal great arteries in the parasternal short-axis view. Instead, it shows two circular structures.
 - b. Other views show the PA arising from the LV and the aorta arising from the RV.
 - c. Associated defects (VSD, LVOT obstruction, PS, ASD, and PDA) can be imaged.
 - d. The status of atrial communication, both before and after balloon septostomy, is best evaluated in the subcostal view.
 - e. The coronary arteries can be imaged in most patients in the parasternal and apical views.
6. Natural history and prognosis depend on anatomy.
 - a. Infants with intact ventricular septum are the sickest group, but they demonstrate the most dramatic improvement following PGE₁ infusion or the Rashkind balloon atrial septostomy.
 - b. Infants with VSD or large PDA are the least cyanotic group but are most likely to develop CHF and PVOD (beginning as early as 3 or 4 months of age).
 - c. Combination of VSD and PS allows considerably longer survival without surgery, but repair surgery carries a high risk.
 - d. Cerebrovascular accident and progressive PVOD, particularly in infants with large VSD or PDA, are rare late complications.

Management

Medical

1. Metabolic acidosis, hypoglycemia, and hypocalcemia should be treated if present.

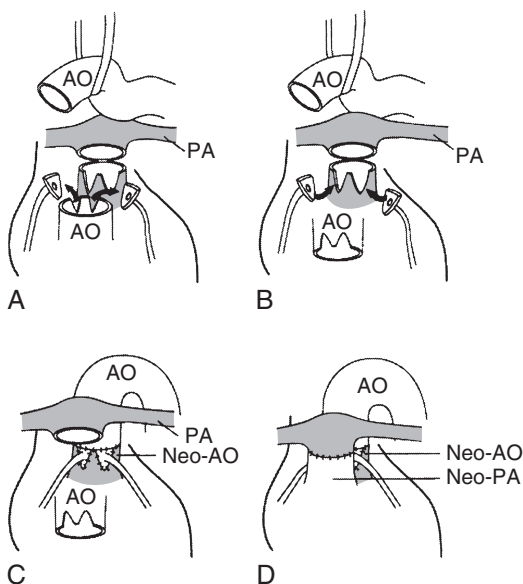
**FIGURE 9-2**

The Rastelli operation. **A**, The PA is divided from the LV, and the cardiac end is oversewn (arrow). **B**, An intracardiac tunnel (arrow) is placed between the large VSD and the aorta. **C**, The RV is connected to the divided PA by an aortic homograft or a valve-bearing prosthetic conduit. AO, aorta; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

2. PGE₁ infusion is started to raise arterial oxygen saturation by reopening the ductus.
3. Administration of oxygen may help raise systemic arterial oxygen saturation by lowering PVR and increasing PBF, with resulting increase in mixing.
4. A therapeutic balloon atrial septostomy (Rashkind procedure) may be performed. The balloon procedure is needed when (a) there is inadequate atrial mixing through the PFO (evidenced by a high Doppler flow velocity of >1 m/sec) and/or (b) immediate surgical intervention is not ready or planned. Occasionally, blade atrial septostomy may be performed for older infants and those for whom the initial balloon atrial septostomy is not successful.
5. Treatment of CHF with diuretics (and digoxin) may be indicated.

Surgical

1. As a definitive surgery, the right- and left-sided structures are switched at the atrial level (Senning operation), at the ventricular level (Rastelli operation), or at the great artery level (arterial switch operation).
 - a. Intraatrial repair surgeries (e.g., Senning operation) are no longer performed, except in rare cases, because of undesirable late complications (such as obstruction to the pulmonary or systemic venous return, TR, arrhythmias, and depressed systemic ventricular (i.e., RV) function).
 - b. Rastelli operation, which redirects the pulmonary and systemic venous blood, is carried out at the ventricular level. It may be carried out in patients with VSD and severe PS. A valved conduit or a homograft is placed between the RV and the PA (Fig. 9-2). This procedure

**FIGURE 9-3**

Arterial switch operation. **A**, The aorta is transected slightly above the coronary ostia, and the main PA is transected at about the same level. The ascending aorta is lifted, and both coronary arteries are removed from the aorta with triangular buttons.

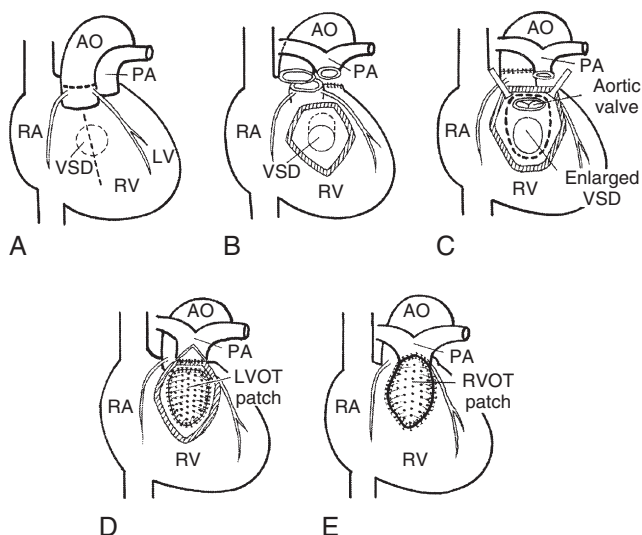
B, Triangular buttons of similar size are made at the proper position in the PA trunk.

C, The coronary arteries are transplanted to the PA. The ascending aorta is brought behind the PA (LeCompte maneuver) and is connected to the proximal PA to form a neo-aorta.

D, The triangular defects in the proximal aorta are repaired, and the proximal aorta is connected to the PA. Note that the neopulmonary artery is in front of the neo-aorta. AO, aorta; PA, pulmonary artery. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

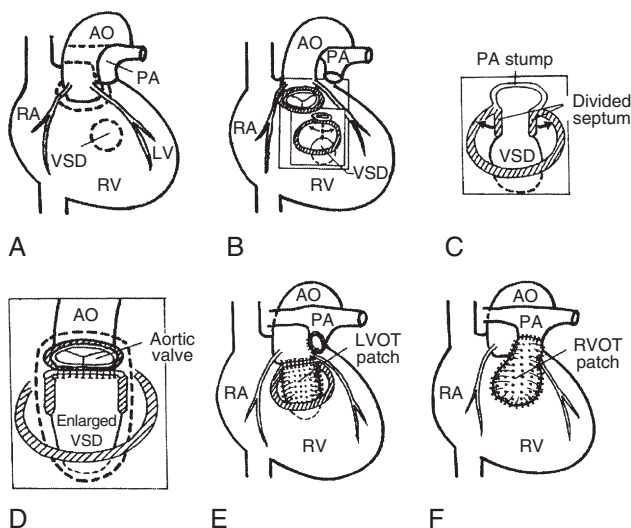
is less popular because of late complications and a high surgical mortality rate (10% and 29%). Two alternative procedures are now available: REV procedure and Nikaidoh procedure (see the following for discussion of these procedures).

- c. Arterial switch operation (ASO) is the procedure of choice (Fig. 9-3). This procedure provides anatomic correction with infrequent complications. For this procedure to be successful, the LV pressure should be near systemic levels at the time of surgery, and therefore should be performed before 3 weeks of age. Possible complications include coronary artery occlusion, supralvalvar PS, supralvalvar neo-aortic stenosis, and AR.
- d. REV procedure (réparation à l'étage ventriculaire) may be performed for patients with associated VSD and severe PS (Fig. 9-4). The procedure comprises the following: (1) infundibular resection to enlarge the VSD,

**FIGURE 9-4**

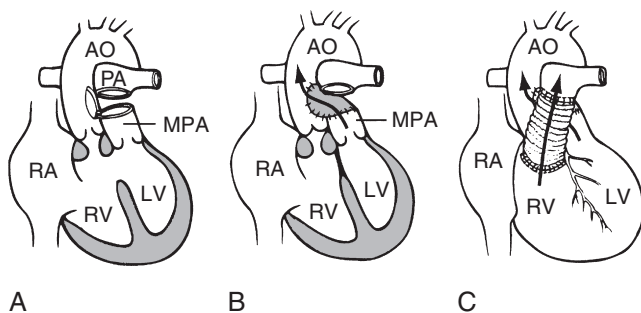
REV procedure for patients with D-TGA + VSD + severe PS. **A**, The broken lines indicate the planned aortic and RV incision sites. The broken circle indicates a VSD. **B**, The aorta and PA have been transected and the RPA is brought anterior to the aorta (Lecompte maneuver). The proximal PA has been oversewn. The VSD is exposed through the right ventriculotomy. Dotted lines indicate the portion of the infundibular septum to be excised to enlarge the VSD. **C**, The aortic valve is well shown by retractors. The broken line indicates the planned site of a patch placement for the LV-AO connection. The transected aorta has been reconnected behind the RPA. **D**, The completed LV-to-AO tunnel is shown. The superior portion of the right ventriculotomy is sutured directly to the posterior portion of the main PA. **E**, A pericardial or synthetic patch is used to complete the RV-to-PA reconstruction. AO, aorta; LV, left ventricle; LVOT, left ventricular outflow tract; PA, pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract; VSD, ventricular septal defect. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- (2) intraventricular baffle to direct LV output to the aorta, (3) aortic transection in order to perform the Lecompte maneuver (by which the RPA is brought anterior to the ascending aorta), and (4) direct RV-to-PA reconstruction by using an anterior patch (see Fig. 9-4). Surgical mortality is 18%.
- e. The Nikaidoh procedure can be performed for patients with associated VSD and severe PS (Fig. 9-5). The repair consists of the following:
 - (1) harvesting the aortic root from the RV (with attached coronary arteries), (2) relieving the LVOT obstruction (by dividing the outlet septum and excising the pulmonary valve), (3) reconstructing the LVOT

**FIGURE 9-5**

Nikaidoh procedure (for patients with D-TGA, VSD, and severe PS). **A**, The circular broken line around the aorta is the planned incision site for aortic root mobilization. The smaller broken circle indicates a VSD. **B**, The aortic root has been mobilized by a circular incision around the aortic root, which leaves an opening in the RV free wall. The main PA is also transected. Through the opening, part of the VSD, ventricular septum, and hypoplastic PA stump are seen. The dotted vertical line in the ventricular septum (in the smaller inset in B) is the planned incision through the infundibular septum. **C**, The incision in the infundibular septum has created a large opening, which includes the PA annulus and stump and the VSD. **D**, The posterior portion of the aorta is directly sutured to the PA stump, which results in a large VSD. This completes translocation of the aorta to the original PA position. The thick oval-shaped broken line that goes through the front of the transected aortic root is the planned site for placement of the LV outflow tract patch, which will direct the LV flow to the aorta. **E**, The completed tunnel is shown (LVOT patch, which directs the LV flow to the aorta). The distal segment of the main PA is fixed to the aorta. Some surgeons use the Lecompte maneuver to bring the RPA in front of the ascending aorta (as shown here). **F**, A pericardial patch is oversewn to complete the RV-to-PA connection (RVOT patch). (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

(with a patch between the aortic root and the VSD), and (4) reconstructing the right ventricular outflow tract (RVOT) with a pericardial patch or a homograft. In the modified Nikaidoh procedure, one or both coronary arteries are moved to a more favorable position as necessary (not shown) and the Lecompte maneuver is also performed (see Fig. 9-5). The hospital mortality is less than 10%.

**FIGURE 9-6**

Damus-Kaye-Stansel operation for D-TGA + VSD + subaortic stenosis. **A**, The MPA is transected near its bifurcation. An appropriately positioned and sized incision is made in the ascending aorta. **B**, The proximal MPA is anastomosed end to side to the ascending aorta, using either a Dacron tube or Gore-Tex. This channel will direct LV blood to the aorta. The aortic valve is either closed or left unclosed. **C**, Through a right ventriculotomy the VSD is closed, and a valved conduit is placed between the RV and the distal PA. This channel will carry RV blood to the PA. AO, aorta; LV, left ventricle; MPA, main pulmonary artery; PA, pulmonary artery; RA, right atrium; RV, right ventricle. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- f. The Damus-Kaye-Stansel operation may be performed at 1 to 2 years of age in infants with a large VSD and significant subaortic stenosis. In this procedure, the subaortic stenosis is bypassed by connecting the proximal PA trunk to the ascending aorta. The VSD is closed, and a conduit is placed between the RV and the distal PA (see Fig. 9-6). The mortality rate is considerable, ranging from 15% to 30%.
2. The indication, timing, and type of surgical treatment vary greatly from institution to institution. Figure 9-7 is a partial listing of many surgical approaches used for infants with TGA, including the timing.

Follow-Up

1. Patients who receive an arterial switch operation need to be followed for stenosis of the anastomosis sites in the PA and AO, signs of AR, and possible coronary obstruction (such as myocardial ischemia, LV dysfunction, arrhythmias).
2. Limitation of activity may be indicated if arrhythmias or coronary insufficiency is present.

II. CONGENITALLY CORRECTED TRANSPOSITION OF THE GREAT ARTERIES (L-TGA)

Prevalence

Much less than 1% of all CHDs.

Transposition of the great arteries

- **Simple TGA** —————→ ASO (1-3 wk)
- **TGA + other simple defects** —————→ ASO (1-3 wk)
(such as PDA, VSD, dynamic or mild PS) + Repair of other defects
- **TGA** —————→ Shunt operation (\pm) —————→ (1) VSD-AO tunnel
+ **VSD** (early in life) + Rastelli (>1-2 yr), or
+ **severe PS** (2) REV procedure (>6 mo), or
(3) Nikaidoh operation (>1 yr)
- **TGA** —————→ “(Initial B-T shunt [\pm])” —————→ Damus-Kaye-Stansel
+ **large VSD** + VSD closure
+ **subaortic stenosis** + RV-PA connection (1-2 yr)

FIGURE 9-7

Surgical approaches to TGA. ASO, arterial switch operation; BT, Blalock-Taussig; PDA, patent ductus arteriosus; PS, pulmonary stenosis; REV, réparation à l'étage ventriculaire; TGA, transposition of the great arteries; VSD, ventricular septal defect. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

Pathology and Pathophysiology

- Visceroatrial relationship is normal (the RA on the right of the LA). The RA empties into the anatomic LV through the mitral valve, and the LA empties into the RV through the tricuspid valve. For this to occur, the LV lies to the right of the RV (i.e., ventricular inversion). The great arteries are transposed, with the aorta arising from the RV and the PA arising from the LV. The aorta lies to the left of and anterior to the PA (hence L-TGA). The final result is a functional correction in that oxygenated blood coming into the LA goes out the aorta (Fig. 9-8).
- Theoretically, no functional abnormalities exist, but unfortunately most cases are complicated by associated defects. VSD (occurring in 80%) and PS (in 50%) with or without VSD are common, resulting in cyanosis. Regurgitation of the systemic AV valve (tricuspid) occurs in 30% of the patients. Varying degrees of AV block, which are sometimes progressive, and supraventricular tachycardia (SVT) are also frequent.
- The cardiac apex is in the right chest (dextrocardia) in about 50% of patients.

Clinical Manifestations

- Patients with associated defects are symptomatic during the first few months of life with cyanosis (VSD + PS) or CHF (large VSD). Patients without associated defects are asymptomatic.

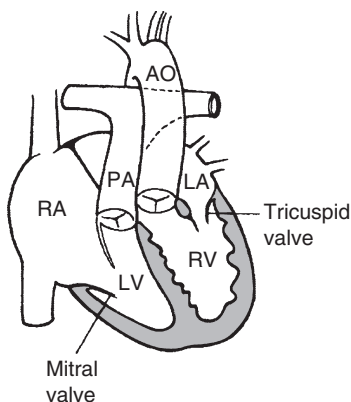
**FIGURE 9-8**

Diagram of congenitally corrected TGA (L-TGA). AO, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

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2. The S2 is single and loud. A grade 2 to 4/6 harsh holosystolic murmur along the LLSB may indicate a VSD or the systemic AV valve (tricuspid) regurgitation. A grade 2 to 3/6 systolic ejection murmur at the ULSB or URSB may indicate PS.
3. Characteristic ECG findings are the absence of Q waves in V5 and V6 and/or the presence of Q waves in V4R or V1. Varying degrees of AV block, including complete heart block, may be present. Atrial and/or ventricular hypertrophy may be present in complicated cases.
4. Chest radiographs may show a characteristic straight left upper cardiac border (formed by the ascending aorta). Cardiomegaly and increased PVMs suggest associated VSD. Dextrocardia is frequent (50%).
5. Two-dimensional echo is diagnostic of the condition and associated defects.
 - a. A “double circle” of the semilunar valves is imaged in the parasternal short-axis view. The posterior circle with no demonstrable coronary arteries is the PA. The aorta is usually anterior to and left of the PA.
 - b. The LV, which has two well-defined papillary muscles, is seen anteriorly and on the right and is connected to the characteristic “fish mouth” appearance of the mitral valve.
 - c. In the apical and subcostal four-chamber views, the LA is seen to connect to the tricuspid valve (which has a more apical attachment to the ventricular septum than the other).
 - d. The anterior artery (aorta) arises from the left-sided morphologic RV, and the posterior artery with bifurcation (PA) arises from the right-sided morphologic LV.
 - e. The situs solitus of the atria is confirmed.

- f. Associated anomalies such as PS (type and severity), VSD (size and location), and straddling of the AV valve should be checked.
6. TR develops in about 30% of patients. Progressive AV conduction disturbances, including complete heart block (up to 30%), may occur.

Management

Medical

1. Treatment of CHF and arrhythmias is indicated, if present.
2. Antiarrhythmic agents are used to treat arrhythmias.

Surgical

1. Palliative procedures: PA banding for uncontrollable CHF due to a large VSD or a B-T shunt for patients with severe PS.
2. Corrective procedures: The presence or absence of TR determines the type of corrective surgery that can be performed, either anatomic repair or classic repair (see Fig. 9-9).
 - a. When there is no TR, a classic repair is done which leaves the anatomic RV as the systemic ventricle.

L-transposition of the great arteries

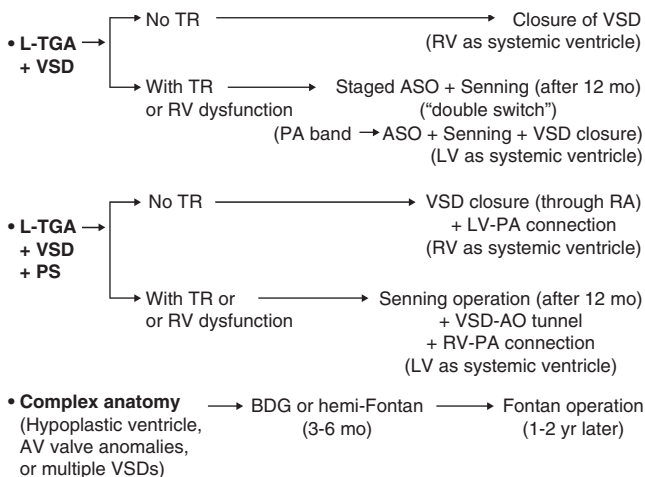


FIGURE 9-9

Surgical summary of L-TGA. AO, aorta; ASO, arterial switch operation; OP, operation; PA, pulmonary artery; PS, pulmonary stenosis (= LV outflow tract obstruction); RV, right ventricle; TGA, transposition of the great arteries; TR, tricuspid regurgitation (= left-sided AV valve regurgitation); VSD, ventricular septal defect. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- b. When there is TR or RV dysfunction, attempts are made to make the LV the systemic ventricle.
 - c. For complex intracardiac anatomy, a staged Fontan-type operation is performed.
3. Other procedures may be necessary:
 - a. Valve replacement for significant TR.
 - b. Pacemaker implantation for either spontaneous or postoperative complete heart block.

Follow-Up

1. Follow-up every 6 to 12 months for a possible progression of AV conduction disturbances, arrhythmias, or worsening TR.
2. Routine pacemaker care is needed if a pacemaker is implanted.
3. Varying degrees of activity restriction may be indicated depending on hemodynamic abnormalities or pacemaker status.

III. TETRALOGY OF FALLOT

Prevalence

10% of all CHD.

Pathology and Pathophysiology

1. The original description of TOF included four abnormalities: a large VSD, RVOT obstruction, RVH, and an overriding of the aorta. However, only two abnormalities are important: a VSD large enough to equalize pressures in both ventricles and an RVOT obstruction (Fig. 9-10).

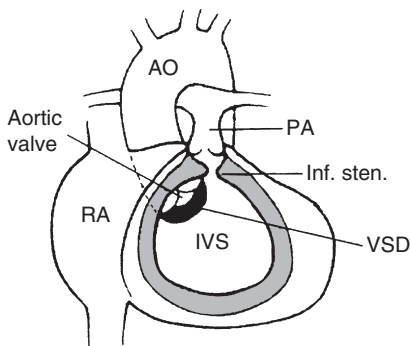


FIGURE 9-10

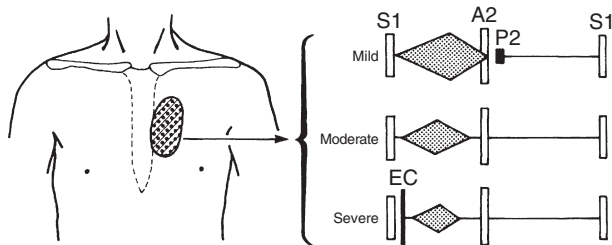
Diagram of TOF. A large subaortic ventricular septal defect (VSD) is present through which aortic cusps are visualized. There is a pulmonary stenosis, which is infundibular, valvular, or a combination. The right ventricular muscle is hypertrophied. An infundibular chamber and hypoplastic main pulmonary artery (PA) are evident. AO, aorta; Inf. sten., infundibular stenosis; IVS, interventricular septum; RA, right atrium. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

The RVH is secondary to the RVOT obstruction and VSD, and the overriding of the aorta varies in degree.

2. The VSD is a perimembranous defect with extension into the infundibular septum. The RVOT may be in the form of infundibular stenosis (50%), pulmonary valve stenosis (10%), or both (30%). The pulmonary annulus and the PA are usually hypoplastic. The pulmonary valve is atretic in 10% of the patients. Abnormal coronary arteries are present in about 5% of the patients, with the most common one being the anterior descending branch arising from the right coronary artery. Right aortic arch is present in 25% of the cases.
3. Because of the nonrestrictive VSD, systolic pressures in the RV and the LV are identical. Depending on the degree of the RVOT obstruction, an L-R, bidirectional, or R-L shunt is present. With a mild PS, an L-R shunt is present ("acyanotic" TOF). With a more severe degree of PS, a predominant R-L shunt occurs (cyanotic TOF). The heart murmur audible in cyanotic TOF originates from the RVOT obstruction, not from the VSD.

Clinical Manifestations

1. Neonates with TOF with pulmonary atresia are deeply cyanotic (see the following separate heading). Most infants with TOF are symptomatic, with cyanosis, clubbing, dyspnea on exertion, squatting, or hypoxic spells. Patients with acyanotic TOF may be asymptomatic.
2. A right ventricular tap and a systolic thrill at the MLSB are usually found. An ejection click of aortic origin, a loud and single S₂, and a loud (grade 3 to 5/6) systolic ejection murmur at the middle and upper LSB are present (Fig. 9-11). Occasionally a continuous murmur representing PDA shunt may be audible in a deeply cyanotic neonate who has TOF with pulmonary atresia. In the acyanotic form, a long systolic murmur resulting from VSD and infundibular stenosis is audible along the entire LSB, and cyanosis is absent.
3. The ECG shows RAD and RVH. BVH may be seen in the acyanotic form.
4. In cyanotic TOF, chest radiographs show normal heart size, decreased PVMs, and a boot-shaped heart with a concave MPA segment. Right aortic arch is present in 25% of the cases. Chest radiographs of acyanotic TOF are indistinguishable from those of a small to moderate VSD.
5. Two-dimensional echo shows a large subaortic VSD and an overriding of the aorta in the parasternal long-axis view. The anatomy of the RVOT, pulmonary valve, pulmonary annulus, and main PA and its branches is imaged in the parasternal short-axis view. Anomalous coronary artery distribution can be imaged accurately. The major concern is to rule out any branch of the coronary artery crossing the RV outflow tract.
6. Children with the acyanotic form of TOF gradually change to the cyanotic form by 1 to 3 years of age. Hypoxic spells may develop in infants (see next section). Brain abscess, cerebrovascular accident, and SBE are rare complications. Polycythemia is common, but relative iron deficiency state (hypochromic) with normal hematocrit may be

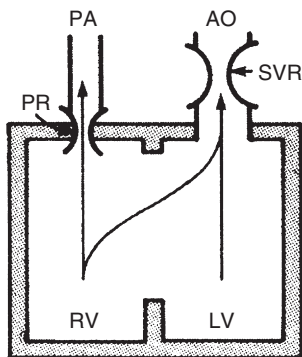
**FIGURE 9-11**

Cardiac findings in cyanotic TOF. A long systolic ejection murmur at the MLSB and ULSB, and a loud, single S2 are characteristic auscultatory findings of TOF. EC, ejection click.

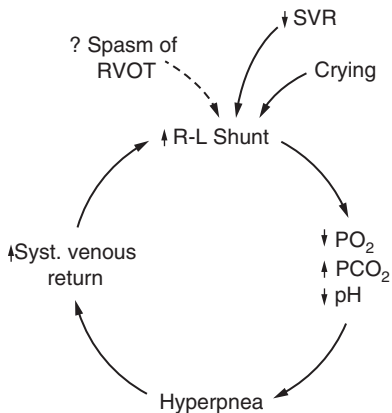
present. Coagulopathies are late complications of a long-standing severe cyanosis.

Hypoxic Spell

1. General description. Hypoxic spell (also called cyanotic spell or “tet” spell) is characterized by (1) a paroxysm of hyperpnea (rapid and deep respiration), (2) irritability and prolonged crying, (3) increasing cyanosis, and (4) decreased intensity of the heart murmur. A severe spell may lead to limpness, convulsion, cerebrovascular accident, or even death. It occurs in young infants, with peak incidence between 2 and 4 months of age. Hypoxic spell requires timely recognition and prompt appropriate treatment.
2. Pathophysiology of hypoxic spell: In TOF, the RV and LV can be viewed as a single pumping chamber, as there are large VSD equalizing pressures in both ventricles (see Fig. 9-12). Lowering the systemic vascular resistance (SVR) or increasing resistance at the RVOT will increase the R-L shunting, and this in turn stimulates the respiratory center to produce hyperpnea. Hyperpnea results in an increase in systemic venous return, which in turn increases the R-L shunt through the VSD, as there is an obstruction at the RVOT. A vicious circle becomes established (Fig. 9-13).
3. Treatment of hypoxic spell: The aim of the treatment is to break the vicious circle of hypoxic spell (as shown in Fig. 9-13). One or more of the following may be employed in decreasing order of preference:
 - a. Pick up the infant and hold in a knee-chest position.
 - b. Morphine sulfate, 0.1 to 0.2 mg/kg SC or IM, suppresses the respiratory center and abolishes hyperpnea.
 - c. Treat acidosis with sodium bicarbonate, 1 mEq/kg IV. This reduces the respiratory center–stimulating effect of acidosis.
 - d. Oxygen inhalation has only limited value, because the problem is a reduced PBF, not the ability to oxygenate.

**FIGURE 9-12**

Simplified concept of TOF that demonstrates how a change in the systemic vascular resistance (SVR) or right ventricular outflow tract obstruction (pulmonary resistance [PR]) affects the direction and the magnitude of the ventricular shunt. AO, aorta; LV, left ventricle; PA, pulmonary artery; RV, right ventricle. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

**FIGURE 9-13**

Mechanism of hypoxic spell. R-L shunt, right-to-left shunt; RVOT, right ventricular outflow tract; SVR, systemic vascular resistance. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- e. With these treatments the infant usually becomes less cyanotic and the heart murmur becomes louder, indicating improved PBF. If not fully responsive with the above measures, the following may be tried.
 - (1) Ketamine, 1 to 3 mg/kg (average of 2 mg/kg) in a slow IV push, works well (by increasing the SVR and sedating the infant).
 - (2) Propranolol, 0.01 to 0.25 mg/kg (average 0.05 mg/kg) in a slow IV push, reduces the heart rate and may reverse the spell.

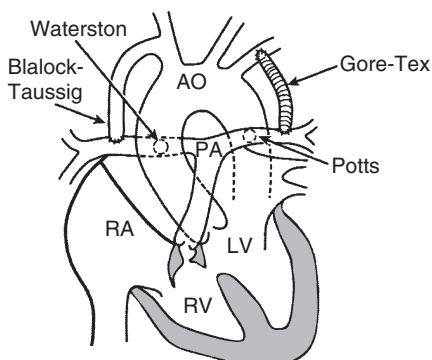
Treatment

Medical

1. Hypoxic spells should be recognized and treated appropriately (as described in the preceding section).
2. Oral propranolol, 2 to 4 mg/kg/day, may be used to prevent hypoxic spells and delay corrective surgery. The beneficial effect of propranolol may be related to its stabilizing action on peripheral vascular reactivity (and thus prevent sudden fall of the SVR), rather than by prevention of RV outflow tract spasm.
3. Detection and treatment of relative iron deficiency state. Anemic children are particularly prone to cerebrovascular accident.

Surgical

1. Palliative procedures are indicated to increase PBF in infants with severe cyanosis or uncontrollable hypoxic spells on whom the corrective surgery cannot safely be performed, and in children with hypoplastic PA on whom the corrective surgery is technically difficult. Different types of systemic-to-pulmonary (S-P) shunts have been performed (Fig. 9-14).
 - a. The Blalock-Taussig (B-T) shunt (anastomosis between the subclavian artery and the ipsilateral PA) may be performed in older infants.
 - b. Gore-Tex interposition shunt (modified B-T shunt) between the subclavian artery and the ipsilateral PA is the procedure of choice in small infants.
 - c. Waterston shunt (anastomosis between the ascending aorta and the right PA) is no longer performed because of many complications following the operation.
 - d. Potts operation (anastomosis between the descending aorta and the left PA) is no longer performed.
2. Complete repair surgery
 - a. Timing:
 - (1) Symptomatic or cyanotic infants with favorable anatomy of the RVOT and PAs may have primary repair at any time after 3 to 4 months of age.
 - (2) Asymptomatic and minimally cyanotic children may have repair between ages 3 and 24 months, depending on the degree of the annular and pulmonary hypoplasia.
 - (3) Mildly cyanotic infants who have had previous shunt surgery may have total repair at 1 to 2 years of age.

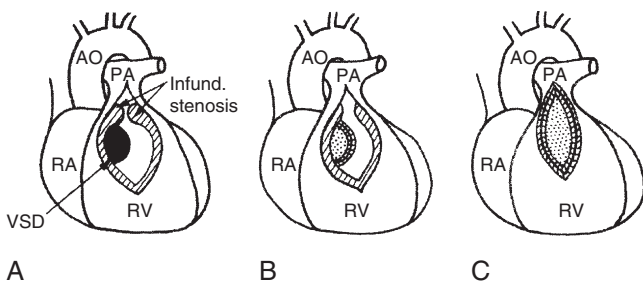
**FIGURE 9-14**

Palliative procedures to increase pulmonary blood flow in patients with cyanosis and decreased PBF. AO, aorta; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- b. Total repair of the defect is carried out under cardiopulmonary bypass. The procedure includes patch closure of the VSD, widening of the RVOT by resection of the infundibular muscle tissue, and usually placement of a fabric patch to widen the RVOT (see Fig. 9-15). Some centers advocate placement of a monocusp valve at the time of initial repair, and other centers advocate pulmonary valve replacement at a later time if indicated.
- c. Surgery for TOF with anomalous anterior descending coronary artery requires placement of a conduit between the RV and PA, which is usually performed after 1 year of age. A B-T shunt may be necessary initially to palliate the patient. Alternatively, when a small conduit is necessary between the RV and the PA, the native outflow tract should be made as large as possible through an atrial approach, so that a “double outlet” (the native outlet and the conduit) results from the RV.

Follow-Up

1. Long-term follow-up every 6 to 12 months is recommended, especially for patients with residual VSD shunt, residual RVOT obstruction, residual PA stenosis, arrhythmias, or conduction disturbances.
2. Later development of significant PR.
 - a. Mild PR is well tolerated for years, but moderate to severe PR can cause RV dilatation and dysfunction and requires surgical insertion of a homograft pulmonary valve.
 - b. RV function is best investigated by MRI; if MRI is contraindicated due to the presence of metallic objects or cardiac pacemaker, a CT can be used.

**FIGURE 9-15**

Total correction of TOF. **A**, Anatomy of TOF showing a large ventricular septal defect (VSD) and infundibular stenosis seen through a right ventriculotomy. Note that the size of the ventriculotomy has been expanded to show the VSD. **B**, Patch closure of the VSD and resection of the infundibular stenosis. **C**, Placement of a fabric patch on the outflow tract of the right ventricle (RV). AO, aorta; PA, pulmonary artery; RA, right atrium. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- c. **Surgical valve replacement.** The following are suggested criteria for surgical valve replacement in patients with moderate to severe PR.
 - (1) RV regurgitation fraction as the primary determinant. In the presence of RV regurgitation fraction $\geq 25\%$, the presence of 2 or more of the following criteria is considered an indication for the procedure (Geva T, 2006): RV end-diastolic volume ≥ 160 ml/m² (normal, <108 ml/m²); RV end systolic volume ≥ 70 ml/m² (normal, <47 ml/m²); LV end-diastolic volume ≥ 65 ml/m²; RV ejection fraction $\geq 45\%$; RV outflow tract aneurysm; and clinical criteria such as exercise intolerance, syncope, presence of heart failure, sustained ventricular tachycardia, or QRS duration ≥ 180 milliseconds.
 - (2) RV volume index as the primary determinant. The presence of RV end-systolic volume index ≥ 80 ml/m² or RV end-diastolic volume index ≥ 163 ml/m² by MRI (Lee C, 2012) is an indication for pulmonary valve replacement. The former index is more important than the latter.
 - (3) The presence of moderate to severe TR, residual ASD or VSD, or severe AR may trigger valve replacement even if the above criteria are not met.
 - (4) If the PR is associated with the stenosis of the main or branch PAs (natural or secondary to shunt operations), the PA stenosis should be relieved first by balloon and/or stent procedure, which may improve PR.
- d. **Nonsurgical percutaneous pulmonary valve implantation.** This technique developed by Bonhoeffer et al has been used successfully, marketed as the Melody transcatheter pulmonary valve (Medtronic,

Minneapolis). Further experiences with this technique may lower the threshold of indication (listed above) for pulmonary valve replacement.

3. Varying levels of activity limitation may be indicated.
4. Some children develop late arrhythmias. Ventricular tachyarrhythmias should be treated aggressively because they may result in sudden death.

IV. TETRALOGY OF FALLOT WITH PULMONARY ATRESIA

Prevalence

About 10% of patients with TOF.

Pathology and Pathophysiology

1. In this extreme form of TOF, the intracardiac pathology resembles that of TOF in all respects except for the presence of pulmonary atresia.
2. The PBF is more commonly through a PDA (70%) and less commonly through multiple systemic collaterals (30%), which are called multiple aortopulmonary collateral arteries (or MAPCAs). Both PDA and collateral arteries may coexist as the source of PBF. The ductus is small and long and descends vertically from the transverse arch ("vertical" ductus) and connects to the PAs which are usually confluent. The subgroup of MAPCAs is usually associated with nonconfluent PAs, and this subgroup is designated as pulmonary atresia and ventricular septal defect.
3. The central and branch PAs are hypoplastic in most patients but more frequently in patients with MAPCAs than in those with PDA. Incomplete arborization (distribution) of one or both PAs is also more common in patients with nonconfluent PAs than those with confluent PAs.

Clinical Manifestations

1. The patient is cyanotic at birth; the degree of cyanosis depends on whether the ductus is patent and how extensive the systemic collateral arteries are.
2. Usually no heart murmur is audible, but a faint, continuous murmur of PDA may be audible. The S2 is loud and single.
3. The ECG shows RAD and RVH.
4. Chest radiographs show normal heart size, often with a boot-shaped silhouette and a markedly decreased PVM ("black" lung field).
5. Echo studies are diagnostic of the condition, but angiocardiogram is necessary for complete delineation of the pulmonary artery anatomy and the collaterals. Alternatively, MRI may be used for complete anatomic delineation of the aortic collaterals and PA branches.

Management

Medical

1. Intravenous PGE₁ infusion is started to keep the ductus open for cardiac catheterization and in preparation for surgery (see Appendix E for the dosage).
2. Emergency cardiac catheterization or MRI is performed to delineate anatomy of the pulmonary arteries and systemic arterial collaterals.

Surgical

1. Primary surgical repair (closure of the VSD, conduit between the RV and the central PA) is possible only when a central PA of adequate size exists and the central PA connects without obstruction to sufficient regions of the lungs (at least equal to one whole lung). The overall hospital mortality varies between 5% and 20%.
2. Staged repair consists of an initial procedure that increases PBF and induces the growth of the central PA (before 1 or 2 years of age) followed by additional surgical procedure(s) at a later time.
 - a. When there is a *confluence* of central PAs, either a B-T shunt or a PA homograft placement can be performed.
 - (1) A B-T shunt procedure often results in an iatrogenic stenosis of the PA branch. For a very small confluent central PA, a central end-to-side shunt (Mee procedure) can be performed.
 - (2) Initial RVOT reconstruction with a small homograft conduit may need to be replaced with a larger one later. Anastomosis of collateral arteries to the central artery is carried out later. In this case, the VSD may be left open, or closed with a fenestrated patch to maintain an increased PBF (see Fig. 9-16, top row).
 - b. When the central PA is *nonconfluent*, with multiple collaterals supplying different segments of the lungs, a surgical connection between or among the isolated regions of the lungs may be made so they might be perfused from a single source (termed *unifocalization of PBF*), with a surgical mortality rate of 5% to 15% (see Fig. 9-16, bottom row). Later, a conduit between the RV and a newly created central PA can be made.
 - c. Occlusion of systemic collateral arteries is done by coil embolization preoperatively or at the time of surgery.
3. Figure 9-17 summarizes surgical approaches for patients with TOF with pulmonary atresia.

Follow-Up

1. Frequent follow-up is needed to assess the palliative surgery, to decide the appropriate time for further operations, and to determine an appropriate time for conduit replacement.
2. SBE prophylaxis is indicated until a complete repair is accomplished.
3. A certain level of activity restriction is needed for most patients even after surgery.

V. TETRALOGY OF FALLOT WITH ABSENT PULMONARY VALVE

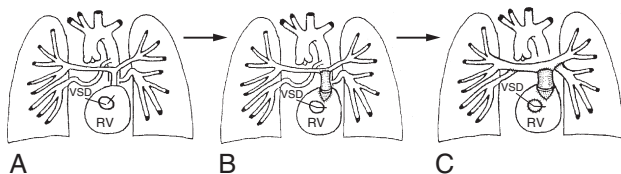
Prevalence

Approximately 2% to 6% of patients with TOF.

Pathology and Pathophysiology

1. The pulmonary valve leaflets are either absent or rudimentary, and the pulmonary annulus is stenotic, usually in association with TOF.

Confluent PA and collaterals



Nonconfluent PA and multiple collaterals

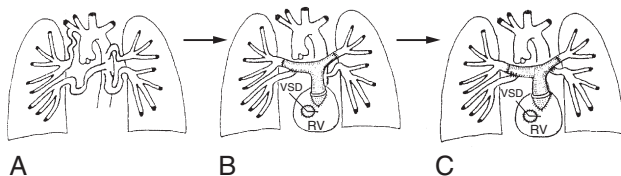
**FIGURE 9-16**

Diagram of multiple-stage repair. **Upper Row (Confluent PA and Collaterals):** **A**, A hypoplastic but confluent central PA and multiple other collateral arteries are shown. **B**, A small RV-to-PA connection is made with a pulmonary homograft (shown with shade), with collaterals left alone. **C**, The pulmonary artery has grown to a larger size and a larger pulmonary homograft has replaced the earlier small one. Collateral arteries are now anastomosed (unifocalized) to the originally hypoplastic PA branches. VSD may be closed at a later time, usually 1 to 3 years of age. The pulmonary homograft is usually replaced with a larger graft at this time. **Bottom Row (Nonconfluent PA and Multiple Collaterals):** **A**, Absent central pulmonary artery and multiple aortic collaterals are shown. **B**, A small pulmonary homograft (6-8 mm internal diameter, shown in shade) is used to establish RV-to-PA connection with some collaterals connected to it (unifocalized) (performed at 3 to 6 mo). Some collaterals are not unifocalized at this time. **C**, The homograft conduit has been replaced with a larger one. Remaining collateral arteries are anastomosed to the pulmonary homograft to complete the unifocalization procedure. VSD is closed with or without fenestration, usually at 1 to 3 years. (Revised from Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

A massive aneurysmal dilatation of the PAs develops during fetal life and compresses the lower end of the developing trachea and bronchi. Postnatally, this produces signs of airway obstruction and respiratory difficulties. Pulmonary complications (e.g., atelectasis, pneumonia), rather than the intracardiac defect, are the usual cause of death when managed medically. In some patients the ductus arteriosus is absent, with a more severe aneurysmal dilatation of the PAs.

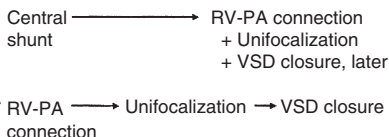
2. Since the annular stenosis is only moderate, a bidirectional shunt is initially present but it becomes predominantly an L-R shunt beyond the newborn period.

Tetralogy of Fallot with pulmonary atresia (or pulmonary atresia and VSD)

■ Confluent PAs with:

- **Favorable PA anatomy** (True PAs providing most PBF with O₂ sat >75%) → Single-stage repair (VSD closure + RV-to-unifocalized PA connection)

• Hypoplastic PAs



■ Nonconfluent PAs + MAPCAs

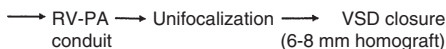


FIGURE 9-17

Surgical approaches for TOF with pulmonary atresia (or pulmonary atresia and VSD). MAPCAs, multiple aorto-pulmonary artery collaterals; PA, pulmonary artery; PBF, pulmonary blood flow; RV-PA, right ventricle-to-pulmonary artery; VSD, ventricular septal defect. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

9

Clinical Manifestations

1. Mild cyanosis may be present in the neonate, but cyanosis disappears and signs of CHF may develop when the PVR falls.
2. A to-and-fro murmur ("sawing-wood sound") at the upper and middle LSB (resulting from PS and PR) is characteristic of the condition. The S2 is loud and single, and RV hyperactivity is palpable.
3. The ECG shows RAD and RVH.
4. Chest radiographs reveal a markedly dilated MPA and hilar PAs. The heart size is either normal or mildly enlarged, and PVMs may be slightly increased. The lung fields may show hyperinflated or atelectatic areas.
5. Echo studies reveal a large, subaortic VSD with overriding of the aorta (as seen in TOF), distally displaced pulmonary annulus (with thick ridges instead of fully developed pulmonary valve leaflets), and gigantic aneurysm of the PA and its branches. The RV is markedly dilated, often with paradoxical motion of the ventricular septum. Doppler studies reveal evidence of stenosis and regurgitation at the annulus.
6. Most infants with severe pulmonary complications (e.g., atelectasis, pneumonia) die during infancy if treated only medically. The surgical mortality of infants with pulmonary complications is as high as 40%. Therefore, surgery should be performed in early infancy before pulmonary complications develop.

Management

Medical

The mortality of medical management is very high. Once the pulmonary symptoms appear, neither surgical nor medical management carries good results.

Surgical

1. Symptomatic neonates should have corrective surgery on an urgent basis. Even asymptomatic infants should have elective primary repair surgery in early infancy. Some use a homograft valve at the pulmonary valve position, and others do not.
2. Alternatively, a two-stage operation can be performed. A tight PA banding is performed to eliminate excessive pulsation of the PA along with a B-T shunt, and a complete repair at a later time (at 2 to 4 years of age).

VI. TOTAL ANOMALOUS PULMONARY VENOUS RETURN

Prevalence

1% of all CHD. There is marked male preponderance (4:1) in the infracardiac type.

Pathology and Pathophysiology

1. The PVs drain into the RA or its venous tributaries, rather than directly into the LA. The defects may be divided into the following four types (Fig. 9-18).
 - a. Supracardiac (50%): The common PV drains into the SVC via the left SVC (vertical vein) and the left innominate vein.
 - b. Cardiac (20%): The common PV drains into the coronary sinus, or the PVs enter the RA separately through four openings.
 - c. Infracardiac (subdiaphragmatic) (20%): The common PV drains to the portal vein, ductus venosus, hepatic vein, or IVC.
 - d. Mixed type (10%): A combination of different types.

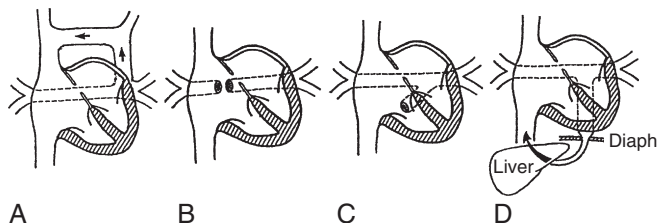


FIGURE 9-18

Anatomic classification of TAPVR. **A**, Supracardiac. **B**, Cardiac, draining into the RA (only 2 pulmonary veins are shown). **C**, Cardiac, draining into the coronary sinus. **D**, Infracardiac.

2. An ASD is necessary for survival. The left side of the heart is relatively small. There is an obstruction of the pulmonary venous return in some patients, especially with the infracardiac type.
3. Pulmonary and systemic venous bloods are completely mixed in the RA. Blood then goes to the LA through an ASD as well as to the RV. Thus, oxygen saturations in the systemic and pulmonary circulations are the same, with resulting systemic arterial desaturation.
4. The level of systemic arterial oxygen saturation is proportional to the amount of PBF. When there is no obstruction to PV return (as seen in most of the supracardiac and cardiac types), pulmonary venous (PV) return is large and the systemic arterial blood is only minimally desaturated. When there is obstruction to PV return (as seen in the infracardiac type), PV return is small and the patient is severely cyanotic.

Clinical Manifestations *without* Obstruction

1. Growth retardation, mild cyanosis, and signs of CHF (tachypnea, tachycardia, and hepatomegaly) are common.
2. Hyperactive RV impulse and characteristic quadruple or quintuple rhythm are present. The S2 is widely split and fixed, and the P2 may be accentuated. A grade 2 to 3/6 systolic ejection murmur is usually present at the ULSB. A mid-diastolic rumble is always present at the LLSB (resulting from relative stenosis of the tricuspid valve).
3. The ECG shows RAD, RVH (rsR' pattern in V1), and occasional RAH.
4. Chest radiographs show moderate to marked cardiomegaly (involving RA and RV) with increased PVMs. A "snowman" sign is seen in older infants with the supracardiac type (usually after 4 months of age).
5. Two-dimensional echo is usually diagnostic. It demonstrates the common PV posterior to the LA without direct communication to the LA. A markedly dilated coronary sinus protruding into the LA (seen in TAPVR to the coronary sinus) or dilated left innominate vein and SVC (seen in the supracardiac type) may be imaged. An ASD with an R-L shunt and relatively small LA and LV are imaged.
6. Cardiac catheterization is usually not necessary for diagnosis; it is occasionally done to perform atrial septostomy to improve atrial shunt or to identify a complex mixed type of pulmonary venous return. Alternatively, MRI or cardiac CT can be used for diagnosis in cases of complex mixed type; the former is preferable because it does not use ionizing radiation.
7. CHF, growth retardation, and repeated pneumonias develop by 6 months of age.

Clinical Manifestations *with* Obstruction

1. Marked cyanosis and respiratory distress are present in the neonate.
2. A loud and single S2 and gallop rhythm are present. Heart murmur is usually absent. Pulmonary crackles may be audible.
3. The ECG shows RAD and RVH.

4. The heart size is usually normal on chest radiographs, but the lung fields reveal findings of pulmonary venous congestion or edema.
5. Two-dimensional echo shows relatively hypoplastic LA and LV. Anomalous PV return below the diaphragm can be directly imaged by 2D echo studies.
6. Cardiac catheterization, MRI, or cardiac CT may be used for complete diagnosis.
7. Patients with the infracardiac type rarely survive more than a few weeks without surgery.

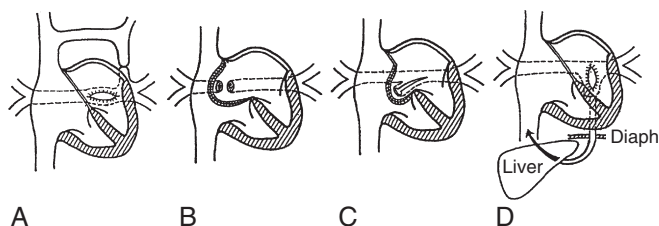
Management of Both Groups of Patients

Medical

1. Intensive anticongestive measures are indicated for the nonobstructive type.
2. Oxygen and diuretics are given for pulmonary edema in infants with the obstructive type. Intubation and ventilator therapy with oxygen and positive end-expiratory pressure (PEEP) may be necessary in infants with severe pulmonary edema.
3. Balloon atrial septostomy to enlarge the interatrial communication may be beneficial at least temporarily.

Surgical

1. There is no palliative procedure. Corrective surgery is indicated for all patients with this condition. Neonates with PV obstruction are operated on soon after the diagnosis, with a surgical mortality rate of about 20%, and infants without PV obstruction are operated on by 4 to 12 months of age, with a mortality rate of 5% to 10%.
2. Surgical techniques used for different types of TAPVR are as follows:
 - a. **Supracardiac Type.** A large, side-to-side anastomosis is made between the common PV and the LA. The vertical vein is ligated. The ASD is closed with a cloth patch (see [Fig. 9-19, A](#)).
 - b. **TAPVR to the Right Atrium.** The atrial septum is excised and a patch is sewn in such a way that the pulmonary venous return is diverted to the LA (see [Fig. 9-19, B](#)).
 - c. **TAPVR to the Coronary Sinus.** An incision is made in the anterior wall of the coronary sinus (“unroofing”) to make a communication between the coronary sinus and the LA. A single patch closes the original ASD and the ostium of the coronary sinus. This will result in the drainage of coronary sinus blood with low oxygen saturation into the LA (see [Fig. 9-19, C](#)).
 - d. **Infracardiac Type.** A large vertical anastomosis is made between the common PV and the LA. The common PV is ligated above the diaphragm (see [Fig. 9-19, D](#)).

**FIGURE 9-19**

Surgical approaches to various types of total anomalous pulmonary venous return (see text). (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

Follow-Up

Follow-up is needed for possible late development of obstruction to PV return (10%) or atrial arrhythmias, including sinus node dysfunction.

9

VII. TRICUSPID ATRESIA

Prevalence

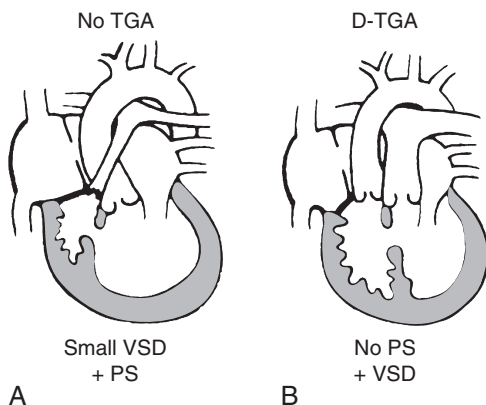
1% to 3% of all CHD in infancy.

Pathology and Pathophysiology

1. The tricuspid valve is absent and the RV and PA are hypoplastic, with decreased PBF. The great arteries are transposed in 30% and normally related in 70% of the cases. Associated defects such as ASD, VSD, or PDA are necessary for survival.
2. In the most common type (50%), a small VSD and PS (with hypoplasia of the PAs) are present, and the great arteries are normally related. In the second most common type (20%), the great arteries are transposed and the pulmonary valve is normal sized (Fig. 9-20).
3. COA or interrupted aortic arch is a frequently associated anomaly, more commonly seen in cases with TGA.
4. All systemic venous return is shunted from the RA to the LA, with resulting dilation and hypertrophy of the RA. The LA and LV are large because they handle both systemic and pulmonary venous returns. The level of arterial saturation is positively related to the level of PBF.

Clinical Manifestations

1. Severe cyanosis, tachypnea, and poor feeding are usual.
2. The S2 is single. A grade 2 to 3/6 systolic regurgitant murmur of VSD is usually present at the LLSB. A continuous murmur of PDA is occasionally audible. Hepatomegaly is present when there is an inadequate interatrial communication or CHF.

**FIGURE 9-20**

The two most common types of tricuspid atresia. In about 50% of patients, the great arteries are normally related and a small VSD and PS are present (**A**). When the great arteries are transposed (about 20% of all cases), a VSD is usually present without PS (**B**). PS, pulmonary stenosis; TGA, transposition of the great arteries; VSD, ventricular septal defect.

3. The ECG shows a characteristic “superior” QRS axis (in most patients without TGA and some patients with TGA), RAH or BAH, and LVH.
4. Chest radiographs show normal or slightly increased heart size and decreased PVMs. A boot-shaped heart with a concave MPA segment may be seen. In infants with TGA, PVMs may be increased.
5. Two-dimensional echo shows atretic tricuspid valve, large LV, diminutive RV, and ASD. The presence or absence of TGA, VSD, PDA, and COA is also imaged. The size of the VSD, the presence and severity of PS, and the presence of TGA should all be investigated. Patients with TGA should be examined for possible subaortic stenosis and COA.
6. Cardiac catheterization with atrial septostomy is indicated when atrial communication is inadequate. Cardiac catheterization is generally recommended before any Fontan-type operation to gain information on the PA anatomy, pressure, and vascular resistance and the LV function.
7. Natural history: Few infants survive beyond 6 months of life without surgical palliation. Occasional patients with increased PBF develop pulmonary hypertension and LV failure, which preclude successful Fontan operation.

Management

Medical

1. Intravenous PGE₁ infusion (see Appendix E for dosage) is indicated in cyanotic neonates to maintain the patency of the ductus before planned cardiac catheterization.
2. The balloon atrial septostomy (Rashkind procedure) may be performed to improve the R-L atrial shunt.
3. Rarely, patients in CHF require anticongestive measures.
4. Infants with VSD of adequate size and normal PBF need to be followed closely for decreasing oxygen saturation which may be caused by reduction in the size of the VSD.

Surgical

The definitive surgery for tricuspid atresia is a Fontan-type operation. One or more palliative procedures are required before Fontan operation to reduce the risk of the procedure.

1. Ideal candidates for a Fontan operation have normal LV function and low PVR.
 - a. Normal LV function results from prevention of excessive volume overload (by using a relatively small B-T shunt, 3.5 mm for neonates) or pressure loading of the LV (by relieving LV outflow obstruction).
 - b. Low PVR may result from adequate growth of PA branches (by a B-T operation), from preventing distortion of the PA (by placing a shunt into the RPA), or from PA banding in the case of increased PBF.
2. Because the Fontan operation is done for many other complex heart defects, a summary of the Fontan pathway is presented in [Box 9-1](#).
1. Staged surgical procedures
 - a. **Stage 1.** One of the following 3 procedures is performed depending on the situation.
 - (1) A B-T shunt (3.5 mm) to the RPA, in patients with decreased PBF.
 - (2) PA banding is rarely necessary for infants with CHF from increased PBF.
 - (3) Damus-Kaye-Stansel and shunt operation for infants with tricuspid atresia + TGA + restrictive VSD. In this procedure, the main PA is transected, and the distal PA is sewn over. The proximal PA is connected end-to-side to the ascending aorta (similar to [Fig. 9-6](#) done for patients with TGA). A B-T shunt is created to supply blood to the lungs.
 - b. **Stage 2.** As a stage 2 operation, either a bidirectional Glenn shunt or the hemi-Fontan operation is performed in preparation for the final Fontan operation.
 - (1) Bidirectional Glenn operation. An end-to-side SVC-to-RPA shunt (also called bidirectional superior cavopulmonary shunt) is performed by 2.5 to 3 months of age ([Fig. 9-21, A](#)). Any previous B-T shunt is taken down at the time of the procedure. The

BOX 9-1

FONTAN PATHWAY

Stage I. One of the following procedures is done in preparation for a future Fontan operation.

1. Blalock-Taussig shunt, when PBF is small
2. PA banding, when PBF is excessive
3. Damus-Kaye-Stansel + shunt operation (for TA + TGA + restrictive VSD)

Medical follow-up after stage I. Watch for:

- a. Cyanosis (O_2 sat. <75%): cardiac catheterization or MRI to find the cause.
- b. Poor weight gain (CHF from too much PBF): tightening of PA band may be necessary.

Stage II (at 3 to 6 mo).

1. BDG operation or
2. The hemi-Fontan operation

Medical follow-up after stage II. Watch for the following:

- a. A gradual decrease in O_2 saturation (<75%) may be caused by:
 - (1) Opening of venous collaterals
 - (2) Pulmonary AV fistula (due to the absence of hepatic inhibitory factor)
 - Perform cardiac catheterization (to find and occlude venous collaterals) or
 - Proceed with Fontan operation
- b. Transient hypertension 1-2 wk postoperatively: may use ACE inhibitors
- c. Cardiac catheterization by 12 mo. after stage II to assess risk factors.

The following are risk factors for the Fontan operation. Presence of ≥ 2 is a high-risk situation.

- (a) Mean PA pressure >18 mm Hg (or PVR >2 U/m²)
- (b) LV end-diastolic pressure >12 mm Hg (or EF <60%)
- (c) AV valve regurgitation
- (d) Distorted PAs secondary to previous shunt operation

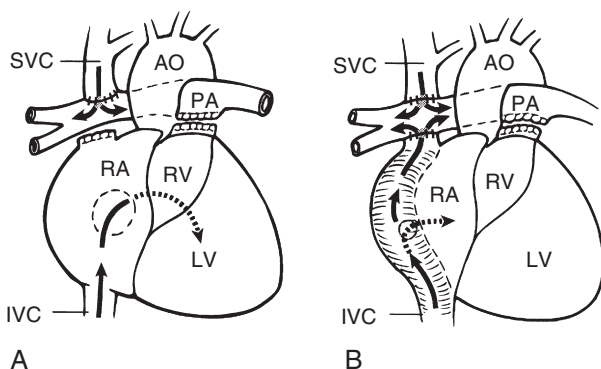
Stage III (Fontan operation) within 1-2 yrs after stage II operation.

1. "Lateral tunnel" Fontan (with 4 mm fenestration); device closure of the fenestration 1-2 yr later, or
2. An extracardiac conduit (usually without fenestration)

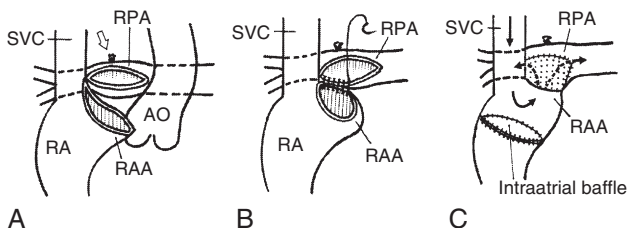
ACE, angiotensin-converting enzyme; AV, atrioventricular (valve) or arteriovenous (fistula); BDG, bidirectional Glenn; CHF, congestive heart failure; EF, ejection fraction; LV, left ventricular; MRI, magnetic resonance imaging; PA, pulmonary artery; PBF, pulmonary blood flow; PVR, pulmonary vascular resistance; TA, tricuspid atresia; TGA, transposition of the great arteries; VSD, ventricular septal defect.

azygos vein and the hemiazygos are divided. The IVC blood still bypasses the lungs. Oxygen saturation increases to about 85%. The surgical mortality rate is between 5% and 10%.

- (2) In the hemi-Fontan operation, an anastomosis is made between the superior part of the right atrial appendage and the lower margin of the central portion of the PA. An intraatrial baffle is placed to direct SVC blood to the PAs. The B-T shunt is taken down and the native pulmonary valve is oversewn (Fig. 9-22).
- c. **Stage 3.** A modified Fontan operation is the definitive procedure for patients with tricuspid atresia. In the Fontan operation, the entire systemic venous return is directed to the pulmonary arteries without an intervening pumping chamber. The Fontan operation is usually completed when the child is around 1 to 2 years of age.

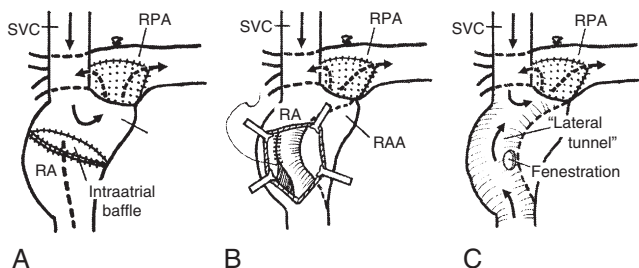
**FIGURE 9-21**

Bidirectional Glenn operation or SVC-RPA anastomosis (**A**) and cavocaval baffle-to-PA connection (Fontan operation) with fenestration (**B**). AO, aorta; IVC, inferior vena cava; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

**FIGURE 9-22**

Hemi-Fontan operation. **A**, A B-T shunt is taken down (arrow). An incision is made in the superior aspect of the right atrial appendage extending it into the SVC and a horizontal incision is made in the RPA. **B**, The lower margin of the RPA incision and the adjacent margin of the incision in the right atrial appendage (RAA) and SVC are connected. **C**, The connection is completed using a pulmonary allograft. An intraatrial patch is placed to direct SVC blood to the PAs. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- (1) The following are risk factors for the Fontan operation: (1) a high PVR ($>2 \text{ U/m}^2$) or high mean PA pressure ($>18 \text{ mm Hg}$); (2) distorted or stenotic PAs secondary to previous shunt operations; (3) poor LV systolic and diastolic functions (LV end-diastolic pressure $>12 \text{ mm Hg}$ or an ejection fraction $<60\%$); and (4) AV valve regurgitation. The presence of two or more of these risk factors constitutes a high-risk situation.

**FIGURE 9-23**

From the hemi-Fontan to Fontan connection. **A**, A vertical incision (heavy broken line) is made in the anterior RA wall. **B**, The intraatrial patch is removed and a lateral tunnel is constructed to direct the IVC blood to the existing conglomerate of RA and RPA. **C**, The direction of blood flow from the SVC and IVC is shown. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- (2) In patients who had the bidirectional Glenn procedure, an intraatrial tubular pathway (termed *cavocaval baffle* or *lateral tunnel*) is created from the orifice of the IVC to the orifice of the SVC. The cardiac end of the SVC is anastomosed to the undersurface of the RPA to complete the operation (see Fig. 9-21, B). Some centers routinely use “fenestration” (4-6 mm) in the baffle, and others use it only in high-risk patients. Some centers recommend device closure of the fenestration a year or so after the Fontan procedure. Early survival rates have improved to over 90%, with a 10-year survival rate of 70%.
- (3) In patients who had the hemi-Fontan operation, the intraatrial patch is excised and a lateral atrial tunnel is constructed, directing flow from the IVC to the previously created amalgamation of the SVC with the RPA (see Fig. 9-23).
- (4) Alternative to a lateral tunnel, an extracardiac conduit may be used to complete the Fontan operation. Extracardiac conduit has a very low operative mortality, a lower incidence of early and late arrhythmias, improved hemodynamics, and fewer postoperative complications. On the other hand, the conduit does not have growth potential and it may be associated with a prolonged period of pleural drainage.
- d. Complications of the Fontan-type operation. Early complications of the Fontan operation may include the following.
 - (1) Low cardiac output and/or heart failure.
 - (2) Persistent pleural effusion occurring more often on the right side.
 - (3) Supraventricular arrhythmia occurs in the early postoperative period in 15% of patients.
 - (4) Thrombus formation in the systemic venous pathways.
 - (5) Although rare, acute liver dysfunction (with ALT >1000 U/L) can occur during the first week after surgery.

Tricuspid atresia

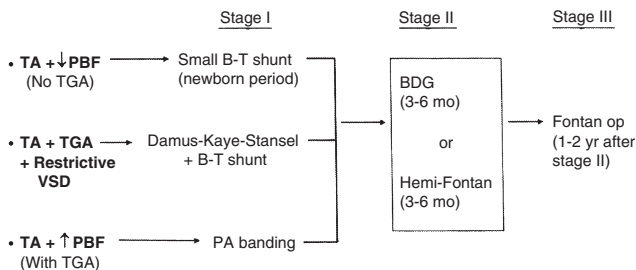


FIGURE 9-24

Surgical approaches in tricuspid atresia. BDG, bidirectional Glenn; B-T, Blalock-Taussig; op, operation; PA, pulmonary artery; PBF, pulmonary blood flow; TA, tricuspid atresia; TGA, transposition of the great arteries; VSD, ventricular septal defect.

(From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

9

Surgical approach for patients with tricuspid atresia is summarized in [Figure 9-24](#).

Post-Fontan Follow-Up

Regular follow-up is necessary for general management and to detect late complications:

1. Patients should maintain a low-salt diet.
2. Medications:
 - a. Some patients need continued digoxin and diuretic therapy.
 - b. An ACE inhibitor (such as captopril or enalapril) is generally recommended, which is an afterload reducer as well as an anti-thrombotic agent (by reducing synthesis of plasminogen activator inhibitor-1 [PAI-1]).
 - c. Aspirin (or even warfarin) is used to prevent thrombus formation. Controversy exists as to whether aspirin is adequate for thrombus prophylaxis as compared to warfarin. A recent international report suggests that aspirin (5 mg/kg/day) is as good as properly controlled warfarin therapy (with target INR at 2.0-3.0). The problem with warfarin is that achieving and maintaining the target level of INR (>2.0) is difficult, especially in children. When the INR levels are inadequately controlled (less than 2.0), the risk of thrombosis appears higher than with aspirin. (Anticoagulation activity is minimal with INR <2.0 and it is almost nonexistent with INR <1.5.) Thus, the ease of aspirin administration and the attendant higher compliance appear to make the antiplatelet dose of aspirin a better choice than warfarin.
3. Some centers recommend device closure of the fenestration a year or so after the Fontan procedure. However, about 20% to 40% of fenestration will close spontaneously in that period of time.

4. Patients should not participate in competitive or contact sports.
5. Antibiotic prophylaxis against SBE should be observed when indications arise.
6. Patients should be advised to live at a low elevation, preferably 4000 feet or less. They should avoid vacationing in high altitudes. High altitudes cause pulmonary vasoconstriction and increase pulmonary vascular resistance. Plasma catecholamine levels and plasma rennin activity also increase. These may lead to Fontan failure, increase Fontan complications (such as protein-losing enteropathy, liver dysfunction), and reduce the rate of long-term survival. Some parts of the Rocky Mountain states and neighboring states have elevations in excess of 4000 feet.
7. Watch for late complications.
 - a. Prolonged hepatomegaly and ascites (which require treatment with digitalis, diuretics, and afterload-reducing agents).
 - b. Late-onset supraventricular arrhythmia continues to increase with longer follow-up (6% at 1 year and 17% at 5 years).
 - c. A progressive decrease in arterial oxygen saturation (which may result from obstruction of the venous pathways, leakage in the intraatrial baffle, or development of pulmonary AV fistula).
 - d. Protein-losing enteropathy can result from increased systemic venous pressure that subsequently causes lymphangiectasis, occurring in 4% of survivors. The prognosis is poor (50% dying within 5 years).

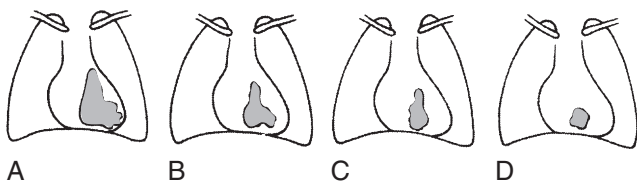
VIII. PULMONARY ATRESIA

Prevalence

Less than 1% of all CHDs or 2.5% of critically ill infants with CHD.

Pathology and Pathophysiology

1. The pulmonary valve is atretic, and the interventricular septum is intact. An interatrial communication (either ASD or PFO) and PDA are necessary for survival.
2. The RV size is variable and is related to survival.
 - a. In the *tripartite type*, all three (inlet, trabecular, and infundibular) portions of the RV are present and the RV is nearly normal in size (Fig. 9-25).
 - b. In the *bipartite type*, the inlet and infundibular portions are present (but the trabecular portion is obliterated).
 - c. In the *monopartite type*, only the inlet portion is present. In the monopartite type, the RV is diminutive, and coronary sinusoids are almost always present (Fig. 9-25).
3. Confluent pulmonary arteries are usually present with PBF provided through a PDA. TR is commonly present.
4. The high pressure in the RV is often decompressed through dilated coronary sinusoids into the left or right coronary artery. Such coronary sinusoids occur only in patients with hypertensive right ventricle but not

**FIGURE 9-25**

Schematic diagram of right ventriculograms that illustrate three types of pulmonary atresia with intact ventricular septum. **A**, Normal right ventricle. **B**, Tripartite type, which shows all three (inlet, trabecular, and infundibular) portions of the RV. **C**, Bipartite type, in which only the inlet and infundibular portions are present. **D**, Monopartite type, in which only the inlet portion of the RV is present (almost always associated with coronary sinusoids). (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

in patients with tricuspid regurgitation. Obstruction of the proximal coronary arteries, which is often present, may cause high surgical mortality.

- Pathophysiology is similar to that of tricuspid atresia. The RA hypertrophies and enlarges to shunt systemic venous return to the LA. The LA and LV handle both systemic and pulmonary venous returns and therefore they enlarge. PBF depends on the patency of PDA; closure of PDA after birth results in death.

Clinical Manifestations

- Severe and progressive cyanosis is present from birth.
- The S2 is single. Usually no heart murmur is present. A soft, continuous murmur of PDA may be audible at the ULNB.
- The ECG shows a normal QRS axis (in contrast to the "superior" QRS axis seen in tricuspid atresia), RAH, and LVH (monopartite type) or occasional RVH (tripartite type).
- The heart size on chest radiographs may be normal or large (with RA enlargement). The MPA segment is concave, with markedly decreased PVMs.
- Two-dimensional echo usually demonstrates the atretic pulmonary valve and hypoplasia of the RV cavity and tricuspid valve. The atrial communication and PDA can be imaged and their size estimated.
- Prognosis is exceedingly poor without neonatal PGE₁ infusion and surgery.

Management

Medical

- As soon as the diagnosis is suspected, intravenous PGE₁ infusion is started to maintain ductal patency (see Appendix E for the dosage). For small premature infants, a prolonged course of PGE₁ infusion may be necessary before surgery is undertaken.

2. Cardiac catheterization and angiocardiography are recommended for most patients to demonstrate coronary sinusoids (by RV angio, demonstrable in 30% to 50% of cases) and to demonstrate possible coronary artery stenosis or interruption (by an ascending aortogram).
3. PDA stenting. In neonates with monopartite RV, who are not likely to be candidates for two-ventricular repair (and are likely to require bidirectional Glenn operation or hemi-Fontan in a few months), some centers use PDA stenting instead of the B-T shunt. PDA stenting is likely to last until the time of the bidirectional Glenn or hemi-Fontan procedure.
4. A balloon atrial septostomy may be performed as part of the cardiac catheterization to improve the R-to-L atrial shunt, but it is recommended only when a two-ventricular repair is considered not possible (due to the presence of RV sinusoids or too small an RV cavity). The balloon atrial septostomy is not performed in patients with the tripartite type. Such patients may become candidates for RVOT patch, in which an elevated RA pressure is important to maximize RV forward output.
5. In patients with membranous atresia, a laser-assisted pulmonary valvotomy with balloon pulmonary valvuloplasty may be a useful alternative to a surgical procedure. (Infundibular atresia is unsuitable for the catheter intervention.)

Surgical

Surgical decision making for this condition depends on the RV size and the presence or absence of RV sinusoids or coronary artery anomalies. The summary of surgical approaches in pulmonary atresia with intact ventricular septum is presented in [Figure 9-26](#).

1. *Adequate RV size:* In patients with tripartite or bipartite RV, a connection is established between the RV and the MPA (either by transannular patch, closed transpulmonary valvotomy, or laser wire and radiofrequency-assisted valvotomy) in preparation for a possible two-ventricular repair. A B-T shunt is performed at the same time.
 - a. If the RV appears to have grown to an adequate size and oxygen saturation is >70% with the B-T shunt closed during cardiac catheterization, two-ventricular repair is performed.
 - b. If the RV size is considered borderline, *one-and-a-half-ventricular repair* may be performed. In this repair, a bidirectional Glenn operation is combined with an RVOT reconstruction.
2. In patients with *monopartite RV* with or without coronary sinusoids, a staged Fontan operation is performed (similar to that described for tricuspid atresia). A B-T shunt is performed initially. A PDA stenting may be an alternative to the B-T shunt.
3. For patients with RV sinusoids, the sinusoids may be left alone or the tricuspid valve is closed (Starnes operation). A B-T shunt or PDA stenting is done initially. A bidirectional Glenn or hemi-Fontan operation is done at 3 to 6 months of age and a Fontan-type operation at 1 to 2 years of age.

Pulmonary atresia with intact ventricular septum

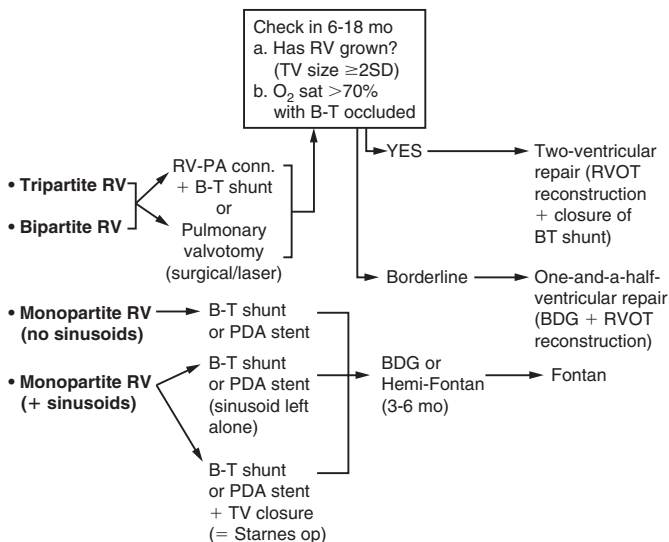


FIGURE 9-26

Surgical approach to pulmonary atresia with intact ventricular septum. BDG, bidirectional Glenn; B-T, Blalock-Taussig; op, operation; RV, right ventricle; RVOT, right ventricular outflow tract; RV-PA conn., right ventricle-to-pulmonary artery connection; TV, tricuspid valve.

Follow-Up

Most patients require close follow-up, because none of the surgical procedures available are curative.

IX. HYPOPLASTIC LEFT HEART SYNDROME

Prevalence

HLHS occurs in 1% of all CHDs.

Pathology and Pathophysiology

1. HLHS includes a group of closely related anomalies characterized by hypoplasia of the LV (in association with atresia or severe stenosis of the aortic and/or mitral valves) and hypoplasia of the ascending aorta and the aortic arch. The LV is small or totally atretic. The atrial septum is intact with a normal patent foramen ovale. A VSD occurs in about 10% of the patients. COA frequently is an associated finding (up to 75%).
2. A high prevalence (up to 29%) of brain abnormalities has been reported, including agenesis of the corpus callosum, holoprosencephaly, microencephaly, and immature cortical mantle.

3. During fetal life the PVR is higher than the SVR, and the dominant RV maintains normal perfusion pressure in the descending aorta through the ductal R-L shunt, even in the presence of the nonfunctioning hypoplastic LV. However, difficulties arise after birth when the ductus closes and the PVR reduces. The end result is a marked decrease in systemic cardiac output and aortic pressure, resulting in circulatory shock and metabolic acidosis. An increase in PBF in the presence of the nonfunctioning LV results in an elevated LA pressure and pulmonary edema.

Clinical Manifestations

1. The neonate is critically ill in the first few hours to days of life, with mild cyanosis, tachycardia, tachypnea, and pulmonary crackles.
2. Poor peripheral pulses and vasoconstricted extremities are characteristic. The S2 is loud and single. Heart murmur is usually absent. Signs of heart failure develop with hepatomegaly and gallop rhythm.
3. The ECG shows RVH. Rarely, LVH pattern is present (because V5 and V6 electrodes are placed over the dilated RV).
4. Chest radiographs show pulmonary venous congestion or pulmonary edema. The heart is only mildly enlarged.
5. Severe metabolic acidosis (caused by markedly decreased cardiac output) in the presence of slightly decreased arterial Po_2 and a normal Pco_2 are characteristic of the condition.
6. Echo findings are diagnostic and usually obviate cardiac catheterization. Severe hypoplasia of the aorta and aortic annulus and the absent or distorted mitral valve are usually imaged. The LV cavity is diminutive. The RV cavity is markedly dilated, and the tricuspid valve is large. A partially constricted PDA may be imaged.
7. Progressive hypoxemia and acidosis result in death without surgery, usually in the first month of life.

Management

Medical

1. The patient should be intubated and ventilated appropriately with oxygen, and metabolic acidosis should be corrected.
2. An intravenous infusion of PGE_1 may produce temporary improvement by reopening the ductus arteriosus (see Appendix E for the dosage).
3. Balloon atrial septostomy may help decompress the LA and temporarily improve oxygenation.
4. A neurologic evaluation, including imaging of the head, should be obtained because of a high prevalence of neurodevelopmental abnormalities seen in this condition. MRI of the head appears to be more sensitive than the head ultrasound scan and the latter shows frequent false positive results.

Surgical

Three options are available in the management of these infants: (1) the Norwood operation (followed by a Fontan-type operation), (2) a hybrid

Hypoplastic
ascending
aorta

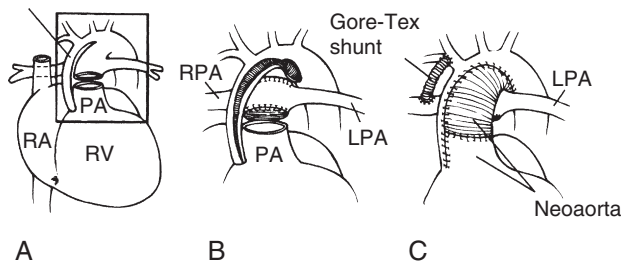


FIGURE 9-27

Schematic diagram of Norwood procedure. **A**, The heart with aortic atresia and hypoplasia of the ascending aorta and aortic arch is shown. The MPA is transected. **B**, The distal PA is closed with a patch. An incision is made in the ascending aorta that extends around the aortic arch to the level of the ductus. The ductus is ligated. **C**, A modified right Blalock-Taussig shunt is created between the right subclavian artery and the RPA as the sole source of pulmonary blood flow. (The Sano central shunt may be used instead of a B-T shunt.) Using an aortic (or pulmonary arterial) allograft (shaded area), the PA is anastomosed to the ascending aorta and the aortic arch to create a large arterial trunk. The procedure to widen the atrial communication is not shown. LPA, left pulmonary artery; PA, pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RV, right ventricle.

operation (followed by a Fontan-type operation), and (3) cardiac transplantation. Only the first two options will be presented because they are more popular than transplantation. A rare subgroup of patients with normal-sized LV (due to a large VSD) can have a two-ventricular repair rather than a Fontan operation.

1. The Norwood Approach.

- a. The first-stage (Norwood) operation is performed in the neonatal period and followed later by the Fontan-type operation. The operation consists of the following procedures (Fig. 9-27): (1) the main PA is divided, the distal stump is closed, and the ductus arteriosus is ligated; (2) a neo-aorta is created by using an allograft that connects the proximal PA and the hypoplastic ascending aorta and aortic arch; (3) pulmonary blood flow is established by either a right-sided B-T shunt or by using a homograft conduit between the RV and PA bifurcation (Sano connection); and (4) excision of the atrial septum. (The Sano central shunt may promote symmetrical growth of the pulmonary arteries and provides a higher aortic diastolic pressure and thus a better coronary artery perfusion than the B-T shunt.) The surgical mortality rate is relatively high (7% to 19%). Post-Norwood medical management may include the use of medications (small-dose diuretic, digoxin (\pm), captopril, and aspirin) and nutritional support.

- b. Second-stage operation for HLHS is either the bidirectional Glenn procedure or the hemi-Fontan procedure. These procedures are performed at 3 to 6 months of age (see section on tricuspid atresia for a description of the procedures).
 - c. A modified Fontan operation is performed at 1 to 2 years of age (see section on tricuspid atresia for a description of the procedures and see [Figs. 9-21, 9-22, and 9-23](#)). Currently, the operative mortality of the Fontan procedure is less than 3%. The overall survival rate after the Fontan operation is better than 95% at follow-up of 50 months.
 - d. Five important hemodynamic and anatomic features considered essential to a successful Fontan operation for patients with HLHS include: (1) unrestrictive interatrial communication, (2) competence of the tricuspid valve, (3) unobstructed PA-to-descending aorta anastomosis (with pressure gradient <25 mm Hg), (4) undistorted PAs and low pulmonary vascular resistance, and (5) preservation of RV function.
2. The Hybrid Approach.
- a. Introduced by Galantowicz et al in 2008, this procedure is now used by many centers as an alternative to Norwood (stage I).
 - (1) Performed in the first week of life, the hybrid approach consists of (1) bilateral PA banding to provide adequate PBF but without causing pulmonary hypertension and (2) insertion of a PDA stent in the same setting to ensure adequate systemic and coronary perfusion (see [Fig. 9-28](#)).
 - (2) It can palliate the infant without the use of cardiopulmonary bypass and delays bidirectional Glenn or hemi-Fontan operation until 3 to 6 months of age. Surgical mortality (2.5%) is much lower than that for the Norwood operation (7% to 19%).
 - (3) As a separate procedure, reliable atrial shunt is established by atrial septostomy.
 - b. Comprehensive stage 2 surgery (performed at 3-6 mo of age) combines the Norwood operation and bidirectional Glenn operation. It includes (1) removal of PDA stent and PA bands, (2) repair of aortic arch and the pulmonary arteries, (3) reimplantation of the diminutive ascending aorta into the pulmonary root, (4) atrial septostomy, and (5) bidirectional Glenn operation. Surgical mortality rate is 8%.
 - c. A Fontan-type operation is performed at age 2 years (as has been described under Tricuspid Atresia).
3. [Figure 9-29](#) summarizes surgical approaches for HLHS.

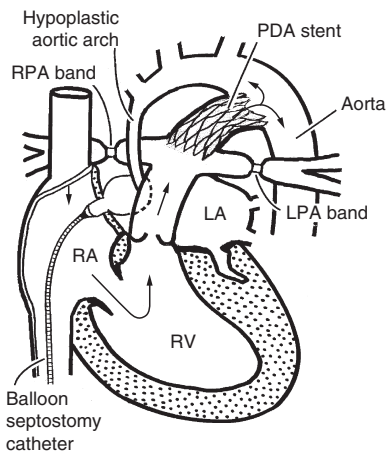
Follow-Up

Postoperative follow-up plans are similar to those described for tricuspid atresia.

X. EBSTEIN ANOMALY

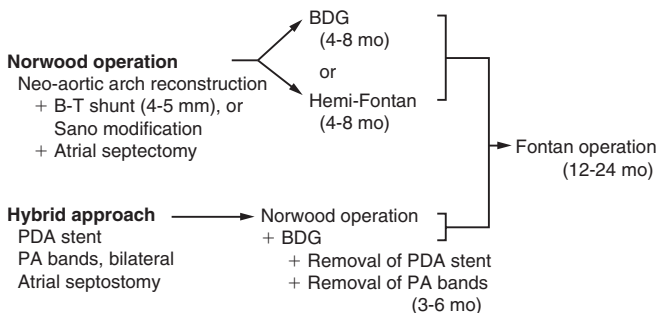
Prevalence

Less than 1% of all CHDs.

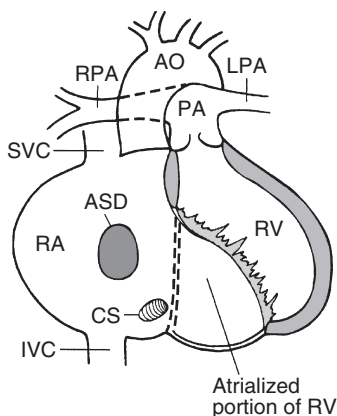
**FIGURE 9-28**

Hybrid Stage I intervention for HLHS. Surgical bands around the right and left pulmonary arteries limit blood flow to the lungs, and a stent in the ductus arteriosus holds it open and maintains adequate blood flow to the body. A balloon atrial septostomy allows unobstructed return of pulmonary venous blood to the right side of the heart. LA, left atrium; LPA, left pulmonary artery; RA, right atrium; RV, right ventricle; RPA, right pulmonary artery.

Hypoplastic left heart syndrome

**FIGURE 9-29**

Surgical approaches to hypoplastic left heart syndrome. BDG, bidirectional Glenn; B-T, Blalock-Taussig. (From Park MK: *Pediatric Cardiology for Practitioners*, ed 5, Philadelphia, Mosby, 2008.)

**FIGURE 9-30**

Ebstein anomaly of the tricuspid valve. There is a downward displacement of the tricuspid valve into the RV. Part of the RV is incorporated into the RA (atrialized portion of the RV). Regurgitation of the tricuspid valve results in an enlargement of the RA. An ASD is usually present. AO, aorta; ASD, atrial septal defect; CS, coronary sinus; IVC, inferior vena cava; LPA, left pulmonary artery; PA, pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RV, right ventricle; SVC, superior vena cava.

Pathology and Pathophysiology

1. The septal and posterior leaflets of the tricuspid valve are displaced into the RV cavity, so that a portion of the RV is incorporated into the RA (atrialized RV), resulting in functional hypoplasia of the RV and TR (Fig. 9-30). An interatrial communication is present, with resulting R-L atrial shunt (and varying degree of cyanosis).
2. The RA is massively dilated and hypertrophied. The RV free wall is often thin. Fibrosis is present in the RV and LV free walls (which may cause ventricular dysfunction).
3. Wolff-Parkinson-White (WPW) preexcitation is frequently associated with the anomaly and predisposes to attacks of SVT.

Clinical Manifestations

1. In severe cases, cyanosis and CHF develop in the first few days of life, with some subsequent improvement. In milder cases, dyspnea, fatigue, and cyanosis on exertion may be present in childhood.
2. The S2 is widely split. Characteristic triple or quadruple rhythm, consisting of split S1, split S2, S3, and S4, is present. A soft regurgitant systolic murmur of TR is usually audible at the LLSB.
3. Characteristic ECG findings are RBBB and RAH. WPW preexcitation, SVT, and first-degree AV block are occasionally present.

4. Chest radiographs may show extreme cardiomegaly, involving principally the RA, and decreased PVMs.
5. Two-dimensional echo shows the apical displacement of the septal leaflet of the tricuspid valve. In the apical four-chamber view, the septal leaflet of the tricuspid valve normally inserts on the ventricular septum slightly more apicalward than the insertion of the mitral valve. In patients with Ebstein's anomaly, this normal displacement is exaggerated. A diagnosis of Ebstein's anomaly is made when the displacement is more than 8 mm/m² of BSA. The tricuspid valve is elongated and dysplastic with resulting TR and occasionally causes RV outflow tract obstruction. A small RV cavity, a large RA, and an ASD (with R-L shunt) are also imaged.
6. Cyanosis of neonates tends to improve as the PVR falls. Patients with less severe forms of the defect may be asymptomatic or only mildly symptomatic. Attacks of SVT are common. Other possible complications include CHF, LV dysfunction with fibrosis, and cerebrovascular accident.

Management

9

Medical

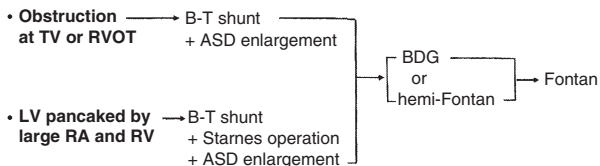
1. In severely cyanotic neonates, intensive treatment with mechanical ventilation, intravenous PGE₁ infusion, inotropic agents, and correction of metabolic acidosis may be necessary.
2. In a less cyanotic child, anticongestive measures with diuretics (with or without digoxin) are indicated if CHF develops.
3. Acute episodes of SVT may be treated most effectively with adenosine. β -blockers are the most appropriate agents for prevention of SVT of undetermined mechanism. For those patients with recurrent SVT due to AV reentrant mechanism, radiofrequency catheter ablation techniques may be indicated.
4. Varying degrees of activity restriction may be necessary.

Surgical

1. Palliative procedures are performed for critically ill neonates.
 - a. Blalock-Taussig shunt (with enlargement of ASD), especially in the presence of RVOT obstruction. A Fontan-type operation is performed later.
 - b. If the LV is "pancaked" by large RV or RA, the Starnes operation (pericardial closure of the tricuspid valve), plication of large atrialized RV, enlargement of ASD, and a Blalock-Taussig shunt using a 4-mm tube may be performed. A Fontan-type operation is performed later.
 - c. Classic Glenn anastomosis (anastomosis of the SVC to the right PA) or its modification may be considered in severely cyanotic infants.
2. Two-ventricular repair (tricuspid valve repair or replacement) is indicated in children with good RV size and function.
 - a. Tricuspid valve repair surgeries (Danielson or Carpentier procedure) are preferable to valve replacement. The Danielson technique plicates the atrialized portion of the RV, narrows the tricuspid orifice

Ebstein anomaly

■ Deeply cyanotic newborns:



■ Asymptomatic children:

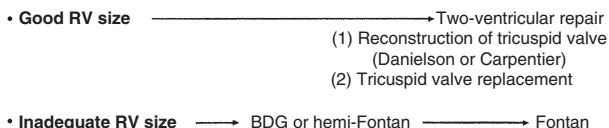


FIGURE 9-31

Surgical approaches for Ebstein anomaly of the tricuspid valve. ASD, atrial septal defect; BDG, bidirectional Glenn; B-T, Blalock-Taussig; LV, left ventricle; RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract; TV, tricuspid valve. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

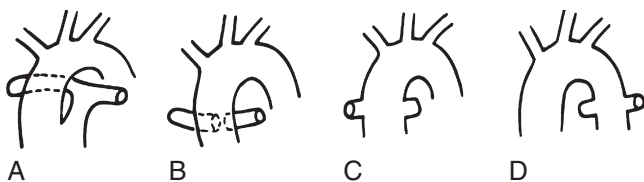
in a selective manner, and results in a monoleaflet tricuspid valve.

The ASD is closed at the time of surgery. The mortality rate of the Danielson procedure is about 5%, which is lower than that for valve replacement. The Carpentier technique is similar to the Danielson technique, but the valvular repair is done in a direction that is at right angles to that used by Danielson. The surgical mortality rate is 15%.

- b. Tricuspid valve replacement (with allograft or heterograft valve) and closure of the ASD is a less desirable surgical approach but may be necessary for 20% to 30% of patients with Ebstein anomaly who are not candidates for reconstructive surgery. The surgical mortality rate ranges from 5% to 20%.
3. One-ventricular repair: For patients with inadequate size of the RV, the Fontan-type operation is usually performed in stages.
4. Other procedures: For patients with WPW syndrome and recurrent SVT, surgical interruption of the accessory pathway is recommended at the time of surgery.
5. Surgical approaches for HLHS are summarized in [Figure 9-31](#).

Follow-Up

1. Frequent follow-up is necessary because of the persistence of arrhythmias after surgery, which occurs in 10% to 20% of patients, and because of possible problems associated with tricuspid valve surgery that require reoperation.
2. The patient should not participate in competitive or strenuous sports.

**FIGURE 9-32**

Anatomic types of persistent truncus arteriosus. **A**, Type I. **B**, Type II. **C**, Type III. **D**, Type IV, or pseudotruncus arteriosus.

XI. PERSISTENT TRUNCUS ARTERIOSUS

Prevalence

Less than 1% of all CHDs.

Pathology and Pathophysiology

1. Only a single arterial trunk (with a truncal valve) leaves the heart and gives rise to the pulmonary, systemic, and coronary circulations. A large VSD is always present. A right aortic arch is present in 30% of patients.
2. Collette and Edwards' classification divides this anomaly into four types (see Fig. 9-32): type I (affects 60%); type II (20%); type III (10%); and type IV (10%). Type IV is not a true persistent truncus arteriosus; it is a severe form of TOF with pulmonary atresia with aortic collaterals supplying the lungs.
3. Coronary artery abnormalities (stenotic coronary ostia, abnormal branching and course) are common, contributing to a high surgical mortality.
4. DiGeorge syndrome with hypocalcemia is present in about 30% of patients. Interrupted aortic arch is seen in 13% (type B interruption between the left carotid and left subclavian arteries).
5. The PBF is usually increased in type I, normal in types II and III, and decreased in type IV. As with other cyanotic CHDs, the level of systemic arterial oxygen saturation is directly related to the amount of PBF. Therefore, with decreased PBF, cyanosis is notable. With increased PBF, cyanosis is minimal, but CHF may develop.

Clinical Manifestations

1. Cyanosis may be noted immediately after birth. Signs of CHF may develop within several weeks.
2. A grade 2 to 4/6 regurgitant systolic murmur (suggestive of VSD) is present along the LSB. A high-pitched diastolic decrescendo murmur of truncal valve regurgitation is occasionally present. An apical diastolic rumble may be audible when PBF is large. Wide pulse pressure and bounding arterial pulses may be present.
3. The ECG shows BVH (70% of patients); RVH or LVH is less common.

4. Chest radiographs usually show cardiomegaly (biventricular and LA enlargement) and increased PVMs. A right aortic arch is seen in 30% of patients.
5. Two-dimensional echo demonstrates a large VSD directly under the truncal valve (similar to TOF). The pulmonary valve cannot be imaged (because it is absent). A large single great artery (truncus arteriosus) arises from the heart. The type of persistent truncus arteriosus and the size of the PAs can be determined. An artery branching posteriorly from the truncus is the PA.
6. Without surgery, most infants die of CHF within 6 to 12 months. Clinical improvement occurs if the infant develops PVOD. Truncal valve regurgitation, if present, worsens with time.

Management

Medical

1. Vigorous anticongestive measures with diuretics and ACE inhibitors are required.
2. Pay attention to the following when DiGeorge syndrome is suspected or confirmed:
 - a. Serum Ca and Mg levels should be obtained.
 - b. Only irradiated blood product should be used.
 - c. Because of the thymus-based immune deficiency, treatment and prophylaxis against pneumococcal and streptococcal infection are important.
 - d. Immunization with live vaccine should be avoided.

Surgical

1. PA banding may be occasionally indicated in small infants with large PBF and CHF, but the mortality is high and the result not satisfactory. Therefore, primary repair of the defect is recommended by many centers.
2. Various modifications of the Rastelli procedure are performed, ideally in the first week of life. The VSD is closed so that the LV ejects into the truncus. An aortic homograft 9 to 11 mm is placed between the RV and the PA. For types II and III, a procedure to join the two PA branches is carried out before connecting it to the distal end of the RV outflow conduit. The mortality rate is as high as 30%.
3. A regurgitant truncal valve is preferably repaired, rather than replaced.

Follow-Up

1. Follow-up every 4 to 12 months is required to detect late complications or problems.
 - a. Truncal valve insufficiency may develop or progress.
 - b. A small conduit needs to be replaced with a larger one, usually by 2 to 3 years of age.
 - c. Calcification of the valve in the conduit may occur within 1 to 5 years.
 - d. Ventricular arrhythmias may develop because of right ventriculotomy.
2. The patient should not participate in competitive or strenuous sports.

XII. SINGLE VENTRICLE

Prevalence

Single ventricle occurs in <1% of all CHDs.

Pathology and Pathophysiology

1. Both AV valves empty into a common main ventricular chamber (double-inlet ventricle). A rudimentary infundibular chamber communicates with the main chamber through the bulboventricular foramen (BVF). One great artery arises from the main chamber, and the other usually arises from the rudimentary chamber. If the main chamber has anatomic characteristics of the LV (80%), it is called double-inlet LV. If the main chamber has anatomic characteristics of the RV, it is called double-inlet RV. Rarely, both atria empty via a common AV valve into the main chamber (common-inlet ventricle).
2. Either D- or L-TGA is present in 85% of patients, and pulmonary stenosis or atresia is present in 50% of patients. COA and interrupted aortic arch are also common.
3. The most common form of single ventricle is double-inlet LV with L-TGA in which the aorta arises from the rudimentary chamber (Fig. 9-33).
4. The bulboventricular foramen (BVF) frequently becomes obstructive, with resulting increase in PBF and decreasing systemic blood flow. This

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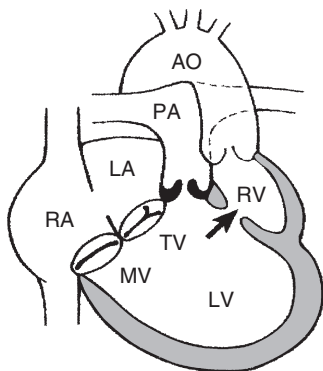


FIGURE 9-33

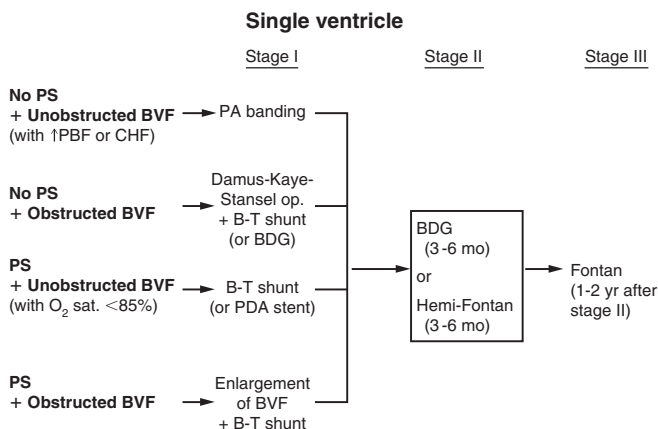
The most common form of single ventricle. The single ventricle is anatomic LV. The great arteries have L-transposition. Stenosis of the pulmonary valve is present in about 50% of patients (shown as thick valves). The bulboventricular foramen (thick arrow) connects the main and the rudimentary ventricles. This type accounts for 70% to 75% of cases of single ventricle. AO, aorta; LA, left atrium; LV, left ventricle; MV, mitral valve; PA, pulmonary artery; RA, right atrium; RV, right ventricle; TV, tricuspid valve.

has important hemodynamic and surgical implications (see Surgical Management).

5. In double-inlet RV, either asplenia or polysplenia with straddling and/or overriding of the AV valves is common.
6. There is a complete mixing of systemic and pulmonary venous blood in the ventricle, and therefore the oxygen saturation in the aorta and PA are identical. The systemic oxygen saturation is proportional to the amount of PBF. With decreased PBF (seen in patients with associated PS), marked cyanosis results. In patients without PS, PBF is large and the patient is minimally cyanotic and may develop CHF.

Clinical Manifestations

1. Cyanosis of a varying degree is present from birth. Symptoms and signs of CHF, failure to thrive, and bouts of pneumonia are commonly reported.
2. Physical findings depend on the magnitude of PBF. With increased PBF, physical findings resemble those of TGA with large VSD. With decreased PBF, physical findings resemble those of TOF.
3. ECG findings may include the following.
 - a. An unusual ventricular hypertrophy pattern with similar QRS complexes across most or all precordial leads (RS, rS, or QR pattern) appears.
 - b. Abnormalities in the Q wave take one of the following forms: (1) Q waves in the RPLs, (2) no Q waves in any precordial leads, or (3) Q waves in both the RPLs and LPLs.
 - c. First- or second-degree AV block or arrhythmias may be present.
4. When PBF is increased, chest radiographs show cardiomegaly and increased PVMs. When PBF is normal or decreased, the heart size is normal and the PVMs are normal or decreased.
5. The diagnostic sign of single ventricle by 2D echo study is the presence of a single ventricular chamber into which two AV valves open. The following anatomic and functional information is important from a surgical point of view.
 - a. Morphology of the single ventricle (e.g., double-inlet LV, double-inlet RV).
 - b. Is D-TGA or L-TGA present?
 - c. Location of the rudimentary outflow chamber, which is usually left and anterior.
 - d. Is the bulboventricular foramen (BVF) adequate or stenotic? The foramen is considered stenotic if the Doppler flow velocity is more than 1.5 m/sec or if the area of the foramen is $<2 \text{ cm}^2/\text{m}^2$. A foramen that is nearly as large as the aortic annulus is considered ideal.
 - e. Presence of PS or AS and the size of the pulmonary arteries.
 - f. Anatomy of the AV valves (stenosis, regurgitation, or straddling).
 - g. The size of the ASD.
 - h. Is PDA, COA, or interrupted aortic arch present?
6. Presence or absence of PS, the size of the BVF, and the presence of AV valve regurgitation affect clinical course. Complete heart block may develop (12%). CHF or arrhythmia can cause death.

**FIGURE 9-34**

Surgical approach for single ventricle. BDG, bidirectional Glenn; B-T, Blalock-Taussig; BVF, bulboventricular foramen; CHF, congestive heart failure; NB, newborn; PBF, pulmonary blood flow; PS, pulmonary stenosis; RPA, right pulmonary artery. (Modified from Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

Management

Medical

1. Neonates with severe PS and those with COA or interrupted aortic arch require intravenous PGE₁ infusion and other supportive measures before surgery.
2. Anticongestive measures with diuretics are indicated if CHF develops.

Surgical

Patients with single ventricle eventually require one-ventricular repair (i.e., Fontan operation) through a staged approach. The purpose of the first-stage operation is to make them acceptable candidates for the bidirectional Glenn or hemi-Fontan procedure. Summary of the surgical approach is shown in [Figure 9-34](#).

1. Initial palliative procedures: The type of initial surgery is influenced by the presence or absence of PS and the size of bulboventricular foramen (BVF).
 - a. No PS + unobstructed BVF (with large PBF and CHF): PA banding is done with a high mortality rate (25% or higher). The banding is done only when the BVF is normal or unobstructed. Obstruction can develop following the PA banding.
 - b. No PS + obstructed BVF: Damus-Kaye-Stansel operation (transection of the MPA, anastomosis of the proximal PA to the aorta) and bidirectional Glenn operation or a B-T shunt.

- c. PS + unobstructed BVF: A B-T shunt or PDA stenting.
- d. PS + obstructed BVF: A B-T shunt and enlargement of the BVF.
2. Second-stage palliative procedures: Either the bidirectional Glenn operation or hemi-Fontan operation (see [Figs. 9-21 and 9-22](#)) is carried out between the ages of 3 and 6 months.
3. The Fontan-type operation is performed at 12 to 24 months of age (see Tricuspid Atresia for detailed discussion of the Fontan procedure).

Follow-Up

Close follow-up is necessary for early and late complications, as discussed in Tricuspid Atresia.

XIII. DOUBLE-OUTLET RIGHT VENTRICLE (DORV)

Prevalence

Less than 1% of all CHDs.

Pathology and Pathophysiology

1. The aorta and the PA arise side by side from the RV. The only outlet from the LV is a large VSD. The aortic and pulmonary valves are at the same level. Subaortic and subpulmonary conuses separate the aortic and pulmonary valves from the tricuspid and mitral valves, respectively. DORV may be subdivided according to the position of the VSD and further by the presence of PS ([Fig. 9-35](#)).
 - a. Subaortic VSD (occurring in 50% to 70% of the patients) ([Fig. 9-35, A](#))
 - b. Subpulmonary VSD (Taussig-Bing anomaly) ([Fig. 9-35, B](#))
 - c. Subaortic VSD + PS (50% of patients with subaortic VSD) ([Fig. 9-35, C](#))
 - d. Doubly committed VSD
 - e. Remote VSD

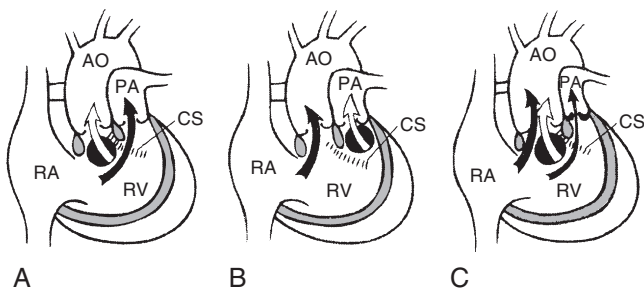


FIGURE 9-35

Three representative types of DORV, viewed with the RV free wall removed.

A, Subaortic VSD. **B**, Subpulmonary VSD (Taussig-Bing anomaly). **C**, Subaortic VSD with PS. Doubly committed and remote VSDs are not shown. AO, aorta; CS, crista supraventricularis; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

2. Pathophysiology of DORV is also determined primarily by the position of the VSD and the presence or absence of PS.
 - a. With subaortic VSD (Fig. 9-35, A), oxygenated blood (open arrow) from the LV is directed to the aorta (AO), and desaturated systemic venous blood (solid arrow) is directed to the pulmonary artery (PA), producing mild or no cyanosis. Clinical pictures resemble those of a large VSD with pulmonary hypertension and CHF.
 - b. With subpulmonary VSD (Fig. 9-35, B), oxygenated blood from the LV is directed to the PA, and desaturated blood from the systemic vein is directed to the aorta, producing severe cyanosis. Thus, clinical pictures resemble those of TGA with CHF.
 - c. In the presence of PS (Fallot type), clinical pictures resemble those of TOF (Fig. 9-35, C).
 - d. With the VSD close to both semilunar valves (doubly committed VSD) or remotely located from these valves (remote VSD), mild cyanosis is present and the PBF is increased.

Clinical Manifestations

1. Subaortic VSD without PS: Physical findings resemble those of a large VSD with pulmonary hypertension and CHF. The ECG often resembles that of ECD ("superior" QRS axis, LAH, RVH, or BVH and occasional first-degree AV block). Chest radiographs show cardiomegaly with increased PVMs and a prominent MPA segment.
2. Subpulmonary VSD (Taussig-Bing malformation): Physical findings resemble those of TGA with severe cyanosis in newborn infants. Signs of CHF supervene later. The ECG shows RAD, RAH, and RVH. LVH may be seen during infancy. First-degree AV block is frequently present. Chest radiographs show cardiomegaly with increased PVMs.
3. Fallot-type DORV with PS: Physical findings are similar to those seen in cyanotic TOF. The ECG shows RAD, RAH, and RVH or RBBB. Chest radiographs show normal heart size (with upturned apex) and decreased PVMs.
4. Echo findings (for all types): Diagnostic 2D echo signs include: (1) both great arteries arising from the RV and running a parallel course in their origin, (2) absence of the LVOT and demonstration of a VSD as the only outlet from the LV, and (3) the mitral-semilunar discontinuity (or absence of normal aortic-mitral continuity).

Management

Medical

Medical treatment of CHF if present.

Surgical

- 1 Palliative procedures
 - a. For infants with remote or multiple VSDs (with large PBF and CHF), a PA banding is occasionally performed. For subaortic, subpulmonary, or doubly committed VSD, primary repair is a better choice.

- b. For infants with subpulmonary VSD, enlarging the ASD by the balloon or blade atrial septectomy is important for decompression of the LA and better mixing of pulmonary and systemic venous blood.
 - c. For infants with subaortic VSD and PS and decreased PBF (Fallot type), a B-T shunt may be indicated.
2. Corrective surgeries
- a. Subaortic VSD and doubly committed VSD: Creation of an intraventricular tunnel between the VSD and the subaortic outflow tract in the neonatal period or at least in early infancy. The surgical mortality rate is <5%.
 - b. Subpulmonary VSD (Taussig-Bing malformation): There are four possible surgical approaches: (1) an intraventricular tunnel between the VSD and the PA (turning it into TGA), plus the arterial switch operation during the first month of life (surgical mortality of 10% to 15%); (2) as in (1) plus the Senning operation (less desirable; surgical mortality above 40%); (c) an intraventricular tunnel between the subpulmonary VSD and the aorta is desirable if technically feasible (mortality of 15%); and (4) creation of a VSD-to-PA tunnel, followed by Damus-Kaye-Stansel operation and RV-to-PA conduit.
 - c. Fallot type: There are three surgical options: (1) an intraventricular VSD-to-aorta tunnel plus RV-to-PA homograft valved conduit at 6 months to 2 years of age, (2) REV procedure (see [Fig. 9-4](#)), or (3) Nikaidoh procedure (see [Fig. 9-5](#)).
 - d. Remote VSD: When possible, an intraventricular tunnel procedure (between inlet VSD and the aorta) is preferred (performed at age 2 to 3 years with a high mortality of 30% to 40%). PA banding is usually needed in infancy to control CHF.
3. Summary of surgical approach is shown in [Fig. 9-36](#).

Follow-Up

Long-term follow-up at 6- to 12-month intervals is necessary to detect late complications (such as the need to reoperate and ventricular arrhythmias).

XIV. HETEROTAXIA (ATRIAL ISOMERISM, ASPLENIA, AND POLYSPLENIA SYNDROMES)

Prevalence

1% to 2% of neonates with symptomatic CHD.

Pathology and Pathophysiology

1. There is a failure of differentiation into the right- and left-sided organs in heterotaxia, with resulting congenital malformations of multiple organ systems.
 - a. *Asplenia syndrome* (right atrial isomerism, Ivemark syndrome) is associated with the absence of the spleen, a left-sided organ, and a tendency to bilateral right-sidedness.
 - b. In *polysplenia syndrome* (left atrial isomerism), multiple splenic tissues with a tendency for bilateral left-sidedness are present.

Double-outlet right ventricle

- **Subaortic VSD or doubly committed VSD** → VSD-AO tunnel (1-6 mo)
- **Fallot type** → B-T shunt (±) →
 1. VSD-AO tunnel + Rastelli (6 mo-2 yr)
 2. REV procedure, or
 3. Nikaidoh procedure
- **Taussig-Bing** → ASD enlargement (balloon/blade) → VSD-PA tunnel + ASO (3-4 mo)
Less desirable possibilities:
 - a. VSD-PA tunnel + Senning
 - b. VSD-AO tunnel (if possible, ± RVOT augmentation)
 - c. VSD-PA tunnel + Damus-Kaye-Stansel + RV-PA conduit
- **Multiple VSD or remote VSD** → PA banding (±) → VSD-AO tunnel (2-3 yr)
 (from multiple VSDs or inlet VSD)
- **Hypoplastic RV or LV** → B-T shunt → BDG or → Fontan
 hemi-Fontan

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FIGURE 9-36

Surgical approach for DORV. AO, aorta; ASD, atrial septal defect; ASO, arterial switch operation; B-T, Blalock-Taussig; PA, pulmonary artery; REV, réparation à l'étage ventriculaire; RV, right ventricle; RVOT, right ventricular outflow tract; RV-PA, RV-to-pulmonary artery; VSD, ventricular septal defect; VSD-AO, VSD-to-aorta; VSD-PA, VSD-to-pulmonary artery. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

2. Noncardiac malformations may help differentiate the two syndromes.
 - a. In asplenia syndrome, bilateral three-lobed lungs (two right lungs) with bilateral eparterial bronchi and various gastrointestinal malformations, including a symmetrical midline liver and malrotation of the intestines, are present. The stomach may be on the right or the left.
 - b. In polysplenia syndrome, bilateral, bilobed lungs (two left lungs) with bilateral, hyparterial bronchi; symmetrical liver (25%); occasional absence of gallbladder; and some degree of intestinal malrotation (80%) are present.
3. Complex cardiac malformations are almost always present, especially with asplenia syndrome. Cardiovascular malformations involve all parts of the heart: systemic and pulmonary veins, the atria, the AV valves, the ventricles, and the great arteries.
 - a. In general, asplenia syndrome has more severe abnormalities of these structures. A normal heart or only minimal malformation of the heart is present in up to 25% of the patients with polysplenia syndrome.
 - b. Bilateral SVCs are common, and anomalies of the pulmonary venous return are usually present.

TABLE 9-1

CARDIOVASCULAR MALFORMATIONS IN ASPLENIA AND POLYSPLENIA SYNDROMES

STRUCTURE	ASPLENIA SYNDROME	POLYSPLENIA SYNDROME
Systemic veins	Normal IVC in all but may be left-sided (35%)	*Absent hepatic segment of IVC with azygos continuation, right or left (85%)
Pulmonary veins	*TAPVR with extracardiac connection (75%), often with PV obstruction	Normal PV return (50%) Right PVs to right-sided atrium; left PVs to left-sided atrium (50%)
Atrium and atrial septum	Bilateral right atria (bilateral sinus node) Primum ASD (100%) + secundum ASD (66%)	Bilateral left atria (no sinus node) Single atrium, primum ASD (60%), or secundum ASD (25%)
AV valve	*Single AV valve (90%)	Normal AV valve (50%); single AV valve (15%)
Ventricles	Single ventricle (50%); two ventricles (50%)	Two ventricles almost always present; VSD (65%); DORV (20%)
Great arteries	*Transposition (70%) (D-TGA, L-TGA) *Stenosis (40%) or atresia (40%) of pulmonary valve	Normal great arteries (85%); transposition (15%) Normal pulmonary valve (60%); pulmonary stenosis or atresia (40%)
ECG	Normal P axis, or in the +90° to +180° quadrant	*Superior P axis (70%)

*Important differentiating points.

- c. Single atrium, secundum ASD, and primum ASD are all common.
 - d. There are either two sinus nodes (seen with asplenia) or no sinus node (seen in polysplenia).
 - e. The coronary sinus is usually absent.
 - f. Single AV valve is common, especially in asplenia.
 - g. Either a single ventricle or VSD is usually present.
 - h. TGA is usually present in asplenia syndrome (70%) and occasionally in polysplenia syndrome (15%).
4. Cardiovascular anomalies that help distinguish these two syndromes are summarized in [Table 9-1](#). The abnormalities with asterisks are particularly helpful but the IVC probably has the most important differential power; the IVC is almost always normal with asplenia syndrome but is interrupted (with azygos continuation) with polysplenia.
5. There is usually a complete mixing of systemic and pulmonary venous blood in the heart because of multiple cardiovascular malformations. When PBF is reduced, as seen with asplenia, severe cyanosis results. When PBF is increased, as in polysplenia syndrome, cyanosis is not intense and CHF often develops.

Clinical Manifestations

1. With asplenia syndrome, cyanosis is often severe shortly after birth. In polysplenia syndrome, signs of CHF may develop during the neonatal period. Heart murmurs of VSD and/or PS are frequently audible.

2. The ECG shows a “superior” QRS axis (due to ECD) in both conditions. An additional “superior” P axis (−30 to −90 degrees) (due to absence of the sinus node) strongly suggests polysplenia syndrome. In asplenia syndrome, the P axis may be either normal or alternating between the left lower and right lower quadrants (because two sinus nodes alternate the pacemaker function). RVH, LVH, or BVH is usually present. Complete heart block occurs in about 10% of the patients with polysplenia syndrome.
3. The heart size is normal or only slightly increased on chest radiographs. The PVMs are either decreased (asplenia) or increased (polysplenia). The heart is in the right or left chest or in the midline (mesocardia). A symmetrical liver (midline liver) is a striking feature of both syndromes.
4. When the systematic approach is used, 2D echo and color flow Doppler studies can detect all or most of the anomalies described under pathology. However, cardiac MRI or CT is usually indicated because almost all of the patients with asplenia syndromes have complex anomalies of pulmonary and systemic venous returns, which cannot always be imaged accurately by echo studies.
5. Without palliative surgical procedures, more than 95% of patients with asplenia syndrome die in the first year of life. Fulminating sepsis is one of the causes of death. Excessive nodal (or junctional) bradycardia with resulting CHF may develop in patients with polysplenia syndrome, requiring a pacemaker therapy.

Management

Medical

1. Intravenous PGE₁ infusion (see Appendix E for dosage) is indicated for severely cyanotic newborn infants with asplenia syndrome to reopen the ductus.
2. Some patients with polysplenia syndrome may need treatment for CHF and occasionally a PA banding.
3. It is important to know which type of isomerism is present for prophylaxis against bacterial infection. The risk of fulminating infection, especially by *Streptococcus pneumoniae*, is high in patients with asplenia syndrome (Red Book, 2012). For asplenic children, the following are recommended.
 - a. Continuous oral antibiotic therapy is recommended regardless of immunization status. Oral penicillin V, 125 mg, twice a day for children <5 yr, and 250 mg, twice a day for children ≥5 yr, is recommended. Some experts recommend amoxicillin (20 mg/kg per day, divided into two doses). Erythromycin is an alternative choice in patients who are allergic to penicillin. Prophylactic penicillin can be discontinued at 5 years of age or continued throughout childhood and into adulthood.
 - b. Immunizations. *Streptococcus pneumoniae* is the most common pathogen that causes bacteremia in asplenic children. Less common causes of bacteremia include *Haemophilus influenzae* type b, *Neisseria meningitidis*, and many others.

- (1) Pneumococcal conjugate and polysaccharide vaccines are indicated for all children with asplenia at the recommended age. (Refer to Red Book, 2012.)
- (2) *H. influenzae* (Hib) immunization should be initiated at 2 months of age, as recommended for otherwise healthy children.
- (3) Two primary doses of quadrivalent meningococcal conjugate vaccine should be administered 2 months apart to children 2 years through adolescence, and a booster dose every 5 years, although its efficacy has not been established.

Surgical

1. For asplenia syndrome
 - a. A B-T shunt is usually necessary because of severe cyanosis. The surgical mortality is high, probably because of regurgitation of the common AV valve and undiagnosed obstructive TAPVR.
 - b. A staged Fontan-type operation can be performed later as outlined under Tricuspid Atresia (but with the surgical mortality as high as 65% because of the AV valve regurgitation).
2. For polysplenia syndrome
 - a. Occasional PA banding is necessary for CHF.
 - b. In some children with polysplenia syndrome, total correction of the defect is possible. If not, a Fontan operation can be performed (with a mortality of about 25%).
 - c. Pacemaker therapy is occasionally required for excessive junctional bradycardia and CHF in children with polysplenia syndrome.

Follow-Up

Similar to follow-up plans outlined under Tricuspid Atresia.

XV. PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN

Prevalence

PPHN (or persistence of the fetal circulation) occurs in approximately 1 in 1500 live births.

Pathology and Pathophysiology

1. This neonatal condition is characterized by persistence of pulmonary hypertension, which in turn causes a varying degree of cyanosis from an R-L shunt through the PDA or patent foramen ovale (PFO). No other underlying CHD is present.
2. Various causes have been identified, but they can be divided into three groups by the anatomy of the pulmonary vascular bed as shown in [Box 9-2](#). In general, pulmonary hypertension caused by the first group is relatively easy to reverse, and that caused by the second group is more difficult to reverse than that caused by the first group. Pulmonary hypertension caused by the third group is the most difficult or impossible to reverse.

BOX 9-2**CAUSES OF PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN**

Pulmonary vasoconstriction in the presence of a normally developed pulmonary vascular bed may be caused by or seen in the following:

Alveolar hypoxia (meconium aspiration syndrome, hyaline membrane disease, hypoventilation caused by central nervous system anomalies)

Birth asphyxia

Left ventricular dysfunction or circulatory shock

Infections (such as group B hemolytic streptococcal infection)

Hyperviscosity syndrome (polycythemia)

Hypoglycemia and hypocalcemia

Increased pulmonary vascular smooth muscle development (hypertrophy) may be caused by the following:

Chronic intrauterine asphyxia

Maternal use of prostaglandin synthesis inhibitors (aspirin, indomethacin) resulting in early ductal closure

Decreased cross-sectional area of pulmonary vascular bed may be seen in association with the following:

Congenital diaphragmatic hernia

Primary pulmonary hypoplasia

3. Varying degrees of myocardial dysfunction often occur in association with PPHN, manifested by a decrease in fractional shortening or TR, which are caused by myocardial ischemia and are aggravated by hypoglycemia and hypocalcemia.

Clinical Manifestations

1. Full-term or postterm neonates are often affected. Symptoms begin 6 to 12 hours after birth, with cyanosis and respiratory difficulties (with retraction and grunting). History of meconium staining or birth asphyxia is often present. A history of maternal ingestion of nonsteroidal antiinflammatory drugs (in the third trimester) may be present.
2. A prominent RV impulse and a single and loud S2 are usually found. Occasional gallop rhythm (from myocardial dysfunction) and a soft regurgitant systolic murmur of TR may be audible. Systemic hypotension may be present with severe myocardial dysfunction.
3. Arterial desaturation is found in blood samples obtained from an umbilical artery catheter. Arterial P_{O_2} is lower in the umbilical artery line than in the preductal arteries (the right radial, brachial, or temporal artery) by 5 to 10 mm Hg, because of an R-L ductal shunt. In severe cases, differential cyanosis may appear (with a pink upper body and a cyanotic lower body). If there is a prominent R-L intracardiac shunt (through PFO or ASD), the preductal and postductal arteries may not show a large P_{O_2} difference.
4. The ECG usually is normal for age but occasional RVH is present. T wave abnormalities suggestive of myocardial dysfunction may be seen.

5. Chest radiographs reveal a varying degree of cardiomegaly with or without hyperinflation or atelectasis. The PVM may appear normal, increased, or decreased.
6. Echo and Doppler studies show no evidence of cyanotic CHD. The only structural abnormality is the presence of a large PDA with an R-L or bidirectional shunt. The atrial septum bulges toward the left due to a higher pressure in the RA, with or without an ASD or PFO. Pulmonary veins are normal (TAPVR can mimic PPHN). The LV dimension may be increased, and the fractional shortening or ejection fraction may be decreased.

Management

1. The goals of therapy are (1) to lower the PVR and PA pressure through the administration of oxygen, the induction of respiratory alkalosis, and the use of pulmonary vasodilators (such as tolazoline); (2) to correct myocardial dysfunction (by dopamine, dobutamine); and (3) to treat associated conditions (e.g., acidosis, hypocalcemia, hypoglycemia).
2. A high-frequency oscillatory ventilator, inhalation nitric oxide (iNO), and employment of ECMO have been shown to be effective in the management of some patients with severe PPHN.

Prognosis

1. Prognosis generally is good for neonates with mild PPHN who respond quickly to therapy. For those requiring a maximal ventilator setting for a prolonged time, the chance of survival is smaller, and many survivors develop bronchopulmonary dysplasia and other complications. Patients with developmental decreases in cross-sectional areas of the pulmonary vascular bed usually do not respond to therapy, and their prognosis is poor.
2. Neurodevelopmental abnormalities may manifest. Patients have a high incidence of hearing loss (up to 50%). An abnormal electroencephalogram (up to 80%) and cerebral infarction (45%) have been reported.

Miscellaneous Congenital Heart Diseases

I. ANEURYSM OF THE SINUS OF VALSALVA

Pathology and Pathophysiology

1. In aneurysm of the sinus of Valsalva, there is a gradual downward protrusion of the aneurysm into a lower-pressure cardiac chamber and it may eventually rupture.
2. Most of the aneurysms arise from the right coronary sinus (80%) and less frequently from the noncoronary sinus (20%).
3. When a sinus of Valsalva aneurysm ruptures, it is called sinus of Valsalva fistula. The fistula communicates most frequently with the RV (75%) and less frequently with the RA (25%).
4. Associated anomalies are common and include VSD (50%), AR (20%), and COA.

Clinical Manifestations

1. An unruptured aneurysm produces no symptoms or signs. Small sinus of Valsalva fistula may develop without symptoms.
2. The aneurysm usually ruptures during the third or fourth decade. The rupture is often characterized by sudden onset of chest pain, dyspnea, a continuous heart murmur over the right or left sternal border, and bounding peripheral pulses. Severe CHF eventually develops.
3. Chest radiographs show cardiomegaly and increased pulmonary vascularity. The ECG may show biventricular hypertrophy (BVH), first- or second-degree AV block, or junctional rhythm.

Management

1. Small to moderate-sized unruptured aneurysms probably do not need surgery.
2. Unruptured aneurysms of the sinus of Valsalva that produce hemodynamic derangement should be repaired.
3. When the aneurysm of sinus of Valsalva has ruptured or is associated with a VSD, prompt operation is advisable.

II. ANOMALOUS ORIGIN OF THE LEFT CORONARY ARTERY (BLAND-WHITE-GARLAND SYNDROME, ALCAPA SYNDROME)

Pathology and Pathophysiology

The left coronary artery (LCA) arises abnormally from the main PA. Postnatal decrease in the PA pressure results in ineffective perfusion of the LCA,

producing ischemia and infarction of the LV that is normally perfused by the LCA.

Clinical Manifestations

1. The newborn patient is usually asymptomatic until the PA pressure falls to a critical level. Symptoms appear at 2 to 3 months of age and consist of recurring episodes of distress (anginal pain), and signs of CHF. Heart murmur usually is absent.
2. Chest radiographs show cardiomegaly. The ECG shows anterolateral myocardial infarction pattern consisting of abnormally deep and wide Q waves, inverted T waves, and ST segment shift in leads I, aVL, and most precordial leads (V2 through V6).
3. Two-dimensional echo with color flow mapping is diagnostic and has replaced cardiac catheterization. The absence of normal LCA arising from the aorta raises the possibility of the condition. Instead, the LCA is seen to connect to the main PA. Color Doppler examination may show retrograde flow into the main PA from the LCA. The right coronary artery may be enlarged. The left ventricle may enlarge with reduced LV systolic function. Increased echogenicity of papillary muscles and adjacent endocardium suggests fibrosis and fibroelastosis.
4. CT scans show high-resolution definition of coronary artery anatomy.

Management

Medical treatment alone carries a very high mortality (80% to 100%). All patients with this diagnosis need surgery.

1. Palliative surgery (simple ligation of the anomalous LCA close to its origin from the PA) may be performed in very sick infants to prevent steal into the PA. This should be followed later by an elective bypass procedure.
2. Most centers prefer definitive surgery unless the patient is critically ill, but the optimal operation remains controversial. One of the following two-coronary system surgeries may be performed.
 - a. Intrapulmonary tunnel operation (Takeuchi repair). Initially a 5- to 6-mm aortopulmonary window is created between the ascending aorta and the MPA at the level of the takeoff of the left coronary artery (LCA). In the posterior wall of the MPA, a tunnel is created that connects the opening of the aortopulmonary window and the orifice of the anomalous left coronary artery. The mortality rate is near 0% but a rate as high as over 20% has been reported. Late complications of the procedure include supravulvar PA stenosis by the tunnel (75%), baffle leak (52%) causing coronary-pulmonary artery fistula, and AR.
 - b. LCA implantation. In this procedure, the anomalous coronary artery is excised from the PA along with a button of PA wall, and the artery is reimplanted into the anterior aspect of the ascending aorta. The early surgical mortality rate is 15% to 20%.
 - c. Tashiro repair. A narrow cuff of the main PA, including the orifice of the left coronary artery, is transected. The upper and lower edges of the cuff

- are closed to form a new left main coronary artery, which is anastomosed to the aorta. The divided main PA is anastomosed end-to-end.
- d. Subclavian-to-left coronary artery anastomosis. In this technique, the end of the left subclavian artery is turned down and anastomosed end-to-side to the anomalous LCA.

III. AORTOPULMONARY SEPTAL DEFECT

Pathology and Pathophysiology

In aortopulmonary septal defect (also known as aortopulmonary [AP] window), a large defect is present between the ascending aorta and the main PA. This condition results from failure of the spiral septum to completely divide the embryonic truncus arteriosus. Unlike persistent truncus arteriosus, two separate semilunar valves are present in this condition.

Clinical Manifestations

1. Clinical manifestations are similar to those of persistent truncus arteriosus and are more severe than those of PDA. CHF and pulmonary hypertension appear in early infancy. Peripheral pulses are bounding, but the heart murmur is usually of the systolic ejection type (rather than continuous murmur) at the base.
2. The natural history of this defect is similar to that of a large untreated PDA, with development of pulmonary vascular obstructive disease in surviving patients.

Management

Prompt surgical closure of the defect under cardiopulmonary bypass is indicated. The surgical mortality rate is very low.

IV. ARTERIOVENOUS FISTULA, CORONARY

Pathology and Pathophysiology

Coronary artery fistulas occur in one of two patterns:

1. True coronary arteriovenous fistula. It represents a branching tributary from a coronary artery coursing along a normal anatomic distribution, with blood emptying into the coronary sinus. This type occurs in only 7% of patients.
2. Coronary artery fistula. In most patients the fistula is the result of an abnormal coronary artery system with aberrant termination. In most cases the fistula terminates in the right side of the heart and the PA (40% in the RV, 25% in the RA, and 20% in the PA).

Clinical Manifestations

1. The patient is usually asymptomatic. A continuous murmur similar to the murmur of PDA is audible over the precordium.
2. The ECG is usually normal, but it may show T wave inversion, RVH, or LVH if the fistula is large. Myocardial infarction pattern can occur. Chest radiographs usually show normal heart size.

3. Echo studies usually suggest the site and type of the fistula. Presence of a massively dilated proximal portion of one coronary artery suggests a coronary artery fistula or an arteriovenous fistula. One can follow the course of the dilated coronary artery to its site of entry.
4. Often selective coronary artery angiography is necessary for accurate diagnosis before intended intervention.

Management

1. A tiny coronary artery fistula to the main PA (coronary artery-to-pulmonary artery fistula) that is detected incidentally by an echo study should be left alone. Spontaneous closure may occur in some small fistulae but some of them may progress and require intervention.
2. Small fistulous connections in the asymptomatic patient may be monitored.
3. For moderate or large coronary artery fistula, transcatheter occlusion is reasonable using coils or other occluding devices.
4. Elective surgery is indicated if not amenable to catheter occlusion. Using cardiopulmonary bypass, the fistula is ligated as proximally as possible without jeopardizing flow in the normal arteries and also ligated near its entrance to the cardiac chamber. The surgical mortality rate is zero to 5%.

V. ARTERIOVENOUS FISTULA, PULMONARY

Pathology and Pathophysiology

1. There is direct communication between the PAs and pulmonary veins (PVs), bypassing the pulmonary capillary circulation. It may take the form of either multiple tiny angiomas (telangiectasis) or a large PA-to-PV communication.
2. About 60% of patients with pulmonary AV fistulas have Osler-Weber-Rendu syndrome. Rarely, chronic liver disease or a previous bidirectional Glenn operation may cause the fistula.

Clinical Manifestations

1. Cyanosis and clubbing are present, with a varying degree of arterial desaturation ranging from 50% to 85%. Polycythemia is usually present. A faint systolic or continuous murmur may be audible over the affected area. The peripheral pulses are not bounding.
2. Chest radiographs show normal heart size (unlike systemic AV fistula). One or more rounded opacities of variable size may be present in the lung fields. The ECG is usually normal.
3. The diagnosis can be made through contrast 2D echo. In this technique, 4 to 10 ml of saline that has been agitated is injected into a peripheral vein while monitoring the appearance of bubbles in the left atrium.
4. CT typically shows one or more enlarged arteries feeding a serpiginous or lobulated mass, and one or more draining veins. Pulmonary

angiography remains the gold standard to determine the position and structure of the fistula prior to intervention.

5. Stroke, brain abscess, and rupture of the fistula with hemoptysis or hemothorax are possible complications.

Management

1. Transcatheter occlusion is recommended for all symptomatic patients and for asymptomatic patients with discrete lesions with feeding arteries ≥ 3 mm in diameter.
2. Diffuse microscopic pulmonary AV malformations are not amenable to transcatheter occlusion. Surgical resection of the lesions, with preservation of as much healthy lung tissue as possible, may be attempted in symptomatic children, but the progressive nature of the disorder calls for a conservative approach.

VI. ARTERIOVENOUS FISTULA, SYSTEMIC

Pathology and Pathophysiology

1. Systemic AV fistulas may be limited to small cavernous hemangiomas or may be extensive. In large AV fistulas, there is direct communication (either a vascular channel or angiomas) between the artery and a vein without the interposition of the capillary bed.
2. The two most common sites of large systemic AV fistulas are the brain and liver.
 - a. In the brain, it is usually a large type occurring in newborns in association with a vein of Galen malformation.
 - b. In the liver, hemangioendotheliomas (densely vascular benign tumors) are more common than fistulous arteriovenous malformation.
3. In the large type, cardiomegaly, tachycardia, and even CHF may result because of decreased peripheral vascular resistance and increased stroke volume.

Clinical Manifestations

1. A systolic or continuous murmur is audible over the affected organ. The peripheral pulses may be bounding. A gallop rhythm may be present with CHF.
2. Chest radiographs show cardiomegaly and increased PVMs. The ECG may show hypertrophy of either or both ventricles.

Management

1. In patients with large cerebral AV fistulas (and CHF), surgical ligation of the affected artery to the brain is rarely possible without infarcting the brain. Many of these infants die in the neonatal period.
2. In hepatic fistulas, surgical treatment is often impossible because they are widespread throughout the liver. However, hemangioendotheliomas often disappear completely.

- a. Large liver hemangiomas have been treated with corticosteroids, aminocaproic acid, local radiation, or partial embolization, but the beneficial effects of these management options are not fully established.
- b. Catheter embolization is becoming the treatment of choice for many symptomatic patients with hepatic AV fistula.

VII. COR TRIATRIATUM

In this rare cardiac anomaly the LA is divided into two compartments by a fibromuscular septum with a small opening, producing obstruction of pulmonary venous (PV) return. Embryologically, the upper compartment is a dilated common PV and the lower compartment is the true LA. Hemodynamic abnormalities of this condition are similar to those of MS in that both conditions produce pulmonary venous and arterial hypertension.

1. Important physical findings include dyspnea, basal pulmonary crackles, a loud P2, and a nonspecific systolic murmur. The ECG shows RVH, and occasional RAH. Chest radiographs show evidence of pulmonary venous congestion or pulmonary edema, prominent MPA segment, and right-sided heart enlargement. Two-dimensional echo is diagnostic. It demonstrates a linear structure within the LA cavity. Degree of obstruction and pulmonary hypertension can be easily estimated by echo study.
2. This is a curable form of pulmonary hypertension. Surgical correction is always indicated. Pulmonary hypertension regresses rapidly in survivors if the correction is made early.

VIII. DEXTROCARDIA AND MESOCARDIA

The terms *dextrocardia* (heart in the right side of the chest) and *mesocardia* (heart in midline of the thorax) express the position of the heart as a whole but do not specify the segmental relationship of the heart. A normally formed heart can be in the right chest because of extracardiac abnormalities. On the other hand, a heart in the right chest may be a sign of a serious cyanotic heart defect. The segmental approach is used to examine the significance of abnormal position of the heart.

A. The Segmental Approach

The heart and the great arteries can be viewed as three separate segments: the atria, the ventricles, and the great arteries. These three segments can vary from their normal positions either independently or together, resulting in many possible sets of abnormalities. Accurate mapping can be accomplished by echo and angiocardiology, but chest radiographs and ECG are helpful also.

1. Localization of the atria.

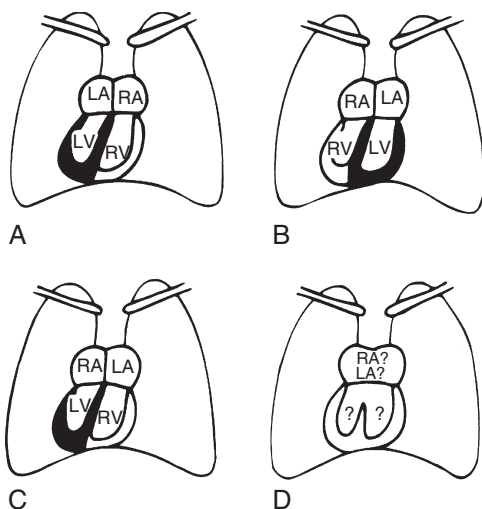
- a. Chest radiographs
 - (1) Right-sided liver shadow and left-sided stomach bubble indicate situs solitus of the atria. Left-sided liver shadow and right-sided stomach bubble indicate situs inversus of the atria.
 - (2) A midline (symmetrical) liver shadow on chest radiograph suggests heterotaxia.

- b. The ECG: The sinoatrial (SA) node is always located in the RA. Therefore, the P axis of the ECG can be used to locate the atria.
 - (1) When the P axis is in the 0 to +90 degrees quadrant, situs solitus of the atria is present.
 - (2) When the P axis is in the +90 to +180 degrees quadrant, situs inversus of the atria is present.
- c. Two-dimensional echo identifies the IVC and/or pulmonary veins. The RA is connected to the IVC, and the LA receives the pulmonary veins.
- 2. **Localization of the ventricles.** Ventricular localization can be accomplished by the ECG and 2D echo.
 - a. ECG: The depolarization of the ventricular septum normally takes place from the embryonic LV to the RV, producing Q waves in the precordial leads that lie over the anatomic LV.
 - (1) If Q waves are present in V5 and V6 but not in V1, D-loop of the ventricle (as in normal persons) is likely.
 - (2) If Q waves are present in V4R, V1, and V2 but not in V5 and V6, L-loop of the ventricles is likely (ventricular inversion, as seen in L-TGA).
 - b. Two-dimensional echo: The tricuspid valve leaflet inserts on the interventricular septum more toward the apex than does the mitral septal leaflet.
 - (1) The ventricle that is attached to the tricuspid valve is the RV.
 - (2) The ventricle that has two papillary muscles is the LV.
- 3. **Localization of the great arteries.** Echo studies can locate the great arteries accurately, but the ECG is not helpful in finding them.

B. Common Types of Displacement

The four most common types of dextrocardia are (1) classic mirror-image dextrocardia, (2) normal heart displaced to the right side of the chest, (3) congenitally corrected TGA, and (4) mal-differentiated ventricle such as seen with asplenia or polysplenia syndrome (Fig. 10-1). All these abnormalities may result in mesocardia. Echo study can make accurate diagnosis of the segmental relationship in dextrocardia or mesocardia. However, chest radiographs and ECGs can be used to deduce the nature of segmental abnormalities, as has been described above.

- 1. Classic mirror-image dextrocardia (Fig. 10-1, A) shows left-sided liver shadow on chest radiographs. The ECG shows the P axis between +90 and +180 degrees and the Q waves in V5R and V6R.
- 2. Normally formed heart shifted toward the right side of the chest (dextroversion) (Fig. 10-1, B) shows the liver shadow on the right on chest radiographs, the P axis between 0 and +90 degrees, and the Q waves in V5 and V6 on the ECG.
- 3. Congenitally corrected L-TGA (Fig. 10-1, C) shows situs solitus of abdominal viscera on chest radiographs. The ECG shows the P axis in the normal quadrant (0 to +90 degrees) and the Q waves on the right precordial leads (V3R, V1, or V2) but no Q waves on V5 and V6.

**FIGURE 10-1**

Examples of common conditions when the apex of the heart is in the right side of the chest. **A**, Classic mirror-image dextrocardia; **B**, Normally formed heart displaced to the right side of the chest; **C**, Congenitally corrected transposition of the great arteries; and **D**, Mal-differentiated ventricle such as seen with asplenia or polysplenia syndrome. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006).

4. Undifferentiated cardiac chambers (Fig. 10-1, D) are often associated with heterotaxia (with complicated cardiovascular defects) and may show midline liver on chest radiographs. The ECG may show the P axis shifting between the 0 to +90 degree quadrant and +90 to +180 degree quadrant in asplenia syndrome (with two sinus nodes). In polysplenia syndrome, the P axis may be superiorly directed (due to ectopic atrial pacemaker). Abnormal Q waves may be seen in the precordial leads.

IX. HEMITRUNCUS ARTERIOSUS

In hemitruncus arteriosus, one of the PAs, usually the right PA, arises from the ascending aorta, rather than the main PA. Hemodynamically, one lung receives blood directly from the aorta (as in PDA) with resulting volume and/or pressure overload, and the other lung receives the entire RV output, resulting in volume overload of that lung. Therefore, pulmonary hypertension of both lungs develops. Associated defects such as PDA, VSD, and TOF are occasionally present.

CHF develops early in infancy, with respiratory distress and poor weight gain. A continuous murmur and bounding pulses may be present. The ECG shows BVH, and chest radiographs show cardiomegaly and increased pulmonary vascular markings.

Early surgical correction (anastomosis of the anomalous PA to the main PA) is indicated.

X. MITRAL STENOSIS, CONGENITAL

Pathology and Pathophysiology

1. Isolated congenital mitral stenosis (MS) is very rare. The mitral obstruction usually occurs at more than one level; it may be at the valve leaflets (fusion of the leaflets), the valve ring itself (hypoplastic valve ring), the papillary muscle (single papillary muscle or “parachute mitral valve”), the chordae (thickened and fused chordae), or the supravalar region (supravalar mitral ring). The mitral commissures are poorly developed.
2. Parachute mitral valve is a condition in which all chordae insert to a single papillary muscle causing obstruction to the entry of blood to the LV.
3. Congenital MS is often part of “Shone complex,” which consists of all or some of the following abnormalities: supravalar mitral ring, MS (of various types as described above), subvalvar and/or valvular AS, aortic arch hypoplasia, and COA.

10

Clinical Manifestations

1. With severe MS, tachypnea and dyspnea, pulmonary venous congestion and/or edema, and right heart failure may develop.
2. With milder stenosis, clinical findings are similar to those described for acquired form (i.e., rheumatic MS) (see Chapter 13).

Management

1. Mild to moderate MS can be managed with the usual anticongestive measures.
2. For infants and children with severe MS, balloon procedure or surgical intervention may be indicated.
 - a. Balloon dilatation of the valve may be attempted but is usually unsuccessful.
 - b. Surgery may be indicated for failed balloon dilatation or severe MR resulting from the balloon procedure.
 - c. Surgically, a supravalar ring can be removed and thickened and fused chordae can be split apart, but commissurotomy is usually not possible. Occasionally, mitral valve replacement may be necessary. A conduit from the LA to the LV is an unusual option.
3. Recurrent atrial fibrillation, thromboembolic phenomenon, and hemoptysis are indications for intervention.

XI. PULMONARY VEIN STENOSIS

This very rare anomaly can be either congenital (or “primary”) or acquired.

A. Primary Pulmonary Vein Stenosis

Pathology

1. Although it can involve a single pulmonary vein (PV), most often multiple veins are involved and the severity can be progressive leading to partial or total obstruction of flow. The number and severity of the stenosis of the PVs involved determine timing and severity of symptoms.
2. More than 50% of patients with PV stenosis have associated cardiac defects.
3. Pathophysiology is similar to that of mitral stenosis, leading to pulmonary edema and pulmonary arterial hypertension.

Clinical Manifestations

1. Infants with the disease present early with respiratory symptoms (tachypnea and recurrent pneumonias).
2. Chest radiographs may show localized or diffuse pulmonary edema depending on the number of PVs involved.
3. Two-dimensional echo studies of the PVs often reveal signs of PV stenosis. Turbulent pulmonary venous flow on color Doppler should raise the suspicion of PV stenosis. Monophasic flow or flow velocities >1.7 m/sec indicate functionally significant stenosis. Normally, early diastolic flow velocity is <1 m/sec. and presystolic flow velocity is much less than that.
4. Diagnosis is established by multidetector CT angiography. Angiography provides the most selective detailed views of the PVs. Radionuclide imaging may demonstrate reduced flow to the affected portion of the lung that receives blood through affected pulmonary vein(s).
5. Prognosis is exceedingly poor in patients with involvement of most or all of the PVs. Patients with only 1 or 2 PVs involved have much more benign courses.

Management

Surgical as well as catheter intervention have a uniformly bad long-term outcome with recurrence within 1 to 6 months. Lung transplantation can be an option in selected patients.

B. Acquired Pulmonary Vein Stenosis

Causes

1. After surgery for TAPVR in children (occurring in about 10% of patients).
2. In adults, the most common cause of PV stenosis is radiofrequency ablation procedures done for treatment of atrial fibrillation. Neoplasm growth, sarcoidosis, or fibrosing mediastinitis are rare causes.

Management

1. Balloon angioplasty of the involved vessels usually leads to a reasonably good initial result but restenosis occurs in $>50\%$ of patients within 1 year.
2. Use of cutting balloon angioplasty and stents may be more successful.

XII. SYSTEMIC VENOUS ANOMALIES

There are wide ranges of abnormalities of the systemic venous system, some of which have little physiologic importance. Others have surgical significance or produce cyanosis. Two well-known anomalies of systemic veins are (1) persistent left SVC and (2) infrahepatic interruption of the IVC with azygos continuation.

A. Anomalies of the Superior Vena Cava

1. Persistent left SVC draining into the RA.
 - a. The left SVC is connected to the coronary sinus as part of the bilateral SVC (Fig. 10-2, A). Rarely, the right SVC is absent (Fig. 10-2, B). A bridging innominate vein is present in 60% of cases.
 - b. Isolated persistent left SVC does not produce symptoms or signs. Cardiac examination is entirely normal. Chest radiographs may show the shadow of the left SVC along the left upper border of the mediastinum. There is a high prevalence of leftward P axis ($+15$ degrees or less, including “coronary sinus rhythm”) on the ECG. Imaging of an enlarged coronary sinus by 2D echo is often the first clue to the diagnosis of persistent left SVC.
 - c. Treatment for isolated persistent left SVC is not necessary.
2. Persistent left SVC draining into the LA (Fig. 10-2, C).
 - a. Persistent left SVC rarely drains into the LA in the absence of the coronary sinus, producing cyanosis (8% of cases). Associated cardiac anomalies, usually of the complex cyanotic type, are almost invariably present.
 - b. Surgical correction is necessary.

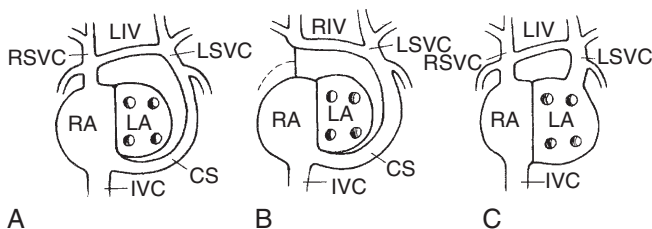
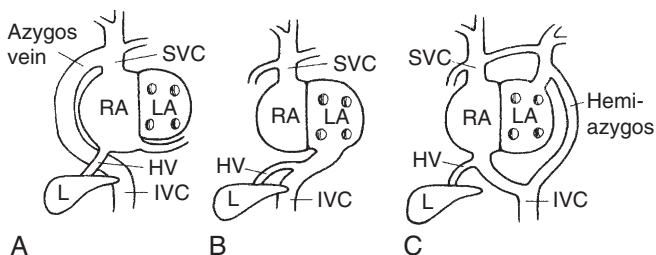


FIGURE 10-2

Schematic diagram of persistent left superior vena cava (LSVC). **A**, LSVC drains via coronary sinus (CS) into the RA. The left innominate vein (LIV) and the right superior vena cava (RSVC) are adequate. **B**, Uncommonly, the RSVC may be atretic. The CS is large because it receives blood from both the right and left upper parts of the body. **C**, The coronary sinus is absent and LSVC drains directly into the LA. The atrial septum is intact. IVC, inferior vena cava; LA, left atrium; RA, right atrium; RIV, right innominate vein.

**FIGURE 10-3**

Schematic diagram of selected abnormalities of the IVC. **A**, Interrupted IVC with azygos continuation, the most common abnormality of the IVC. The hepatic vein (HV) connects directly to the RA. **B**, Right IVC draining into the LA. **C**, Absence of the lower right IVC. The IVC drains into the left superior vena cava and LA and to the RA through the hepatic portion of the IVC. IVC, inferior vena cava; L, liver; LA, left atrium; RA, right atrium; SVC, superior vena cava.

B. Anomalies of the Inferior Vena Cava

1. **Interrupted IVC with azygos continuation.**
 - a. Instead of receiving the hepatic veins and entering the RA, the IVC drains via an enlarged azygos system into the right SVC and eventually to the RA (Fig. 10-3, A). The hepatic veins connect directly to the RA. Bilateral SVC is also common. This type has been reported in about 3% of children with CHDs
 - b. Azygos continuation of the IVC is often associated with complex cyanotic CHDs, including polysplenia syndrome. No case has been reported in association with asplenia syndrome.
 - c. This defect creates difficulties in manipulating catheters during cardiac catheterization and can render surgical correction of an underlying cardiac defect more difficult.
 - d. There is no need for surgical correction of this venous anomaly per se.
2. **IVC connecting to the LA.** This is an extremely rare condition in which the IVC receives the hepatic veins, curves toward the LA, and makes a direct connection with the LA (Fig. 10-3, B), producing cyanosis. Surgical correction is indicated.
3. **Absent right IVC.** Dominant left LVC, in the absence of right IVC, drains into the LA through the left-sided hemiazygos system and persistent left SVC, producing cyanosis (Fig. 10-3, C).

XIII. VASCULAR RING

Prevalence

Vascular ring reportedly constitutes less than 1% of all congenital cardiovascular anomalies, but this is probably an underestimation.


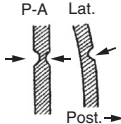
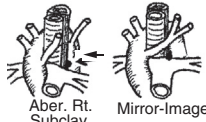
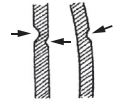


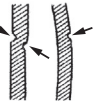

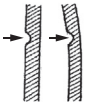
	Anatomy	Ba-Esophag.	Chest Film	Symptoms	Treatment
Double Aortic Arch			Anterior compression of trachea	Respiratory difficulties in early infancy Swallowing dysfunction	Surgical division of the smaller arch
Right Aortic Arch with Left Lig. Arteriosum			Right aortic arch	Mild respiratory difficulties late in infancy Swallowing dysfunction	Surgical division of left lig. arteriosum
Anomalous Innominate Artery		Normal	Anterior compression of trachea	Stridor and/or cough in infancy	Conservative management Surgical suturing of the artery to the sternum (\pm)
Aberrant Right Subclavian Artery				Occasional swallowing dysfunction	Usually no treatment is necessary
"Vascular Sling"			Right-sided emphysema/atelectasis Posterior compression of trachea	Wheezing and cyanotic episodes since birth	Surgical division of the anomalous LPA (from the RPA) and anastomosis to the MPA

FIGURE 10-4

Summary and clinical features of vascular ring. Aber. Rt. Subclav., aberrant right subclavian; Ba-Esophag., barium esophagogram; Lat., lateral view; lig., ligamentum; LPA, left pulmonary artery; MPA, main pulmonary artery; P-A, posteroanterior view; Post., posterior; RPA, right pulmonary artery.

Pathology

1. Vascular ring refers to a group of anomalies of the aortic arch and pulmonary artery that cause respiratory symptoms or feeding problems.
2. The vascular ring may be divided into two groups: complete (or true) and incomplete.
 - a. In complete vascular ring, the abnormal vascular structures form a complete circle around the trachea and esophagus. They include (1) double aortic arch and (2) right aortic arch with left ligamentum arteriosum.
 - b. Incomplete vascular ring comprises vascular anomalies that do not form a complete circle around the trachea and esophagus but do compress these structures. These include (1) anomalous innominate artery, (2) aberrant right subclavian artery, and (3) anomalous left pulmonary artery (“vascular sling”).
3. Pathology of five major vascular rings is presented in the following sections
 - a. **Double aortic arch** is the most common vascular ring (40%) (see Fig. 10-4). The right and left aortic arches completely encircle and compress the trachea and esophagus, producing respiratory distress and feeding problems in early infancy. Both aortic arches give off two branches, each giving off the common carotid and the subclavian arteries. The right aortic arch is usually larger than the left arch. This condition is usually an isolated anomaly but is occasionally associated with CHDs such as TGA, VSD, persistent truncus arteriosus, TOF, and COA.
 - b. **Right aortic arch with left ligamentum arteriosum.** Depending on the morphology of arch branching, different types may occur.
 - (1) In the most frequent form (65%), the right arch first gives off the left carotid artery, then the right carotid artery, followed by the right subclavian artery, and lastly the left subclavian artery (left figure of the anatomy in Fig. 10-4). The ring is completed by a left-sided ligamentum arteriosum connecting the subclavian artery to the left PA. The aberrant left subclavian artery often arises from a retroesophageal diverticulum (called diverticulum of Kommerell). About 10% of this form is associated with an intracardiac defect.
 - (2) In the second type (occurring in about 35%), the left innominate artery originates from the right arch in mirror image fashion as the first branch, followed by the right carotid and right subclavian arteries. A left-sided ductus (or ligament) connects the descending aorta and the proximal left PA (right figure of the anatomy in Fig. 10-4). More than 90% of patients with this anomaly have associated CHDs, notably TOF and persistent truncus arteriosus.
 - c. In **anomalous innominate artery** the artery takes off too far to the left from the arch and compresses the trachea, producing mild respiratory symptoms (see Fig. 10-4). This anomaly is commonly associated with other CHDs such as VSD.

- d. In **aberrant right subclavian artery** the artery arises independently from the descending aorta and courses behind the esophagus, producing mild feeding problems (Fig. 10-4). It is the most common arch anomaly (occurring in 0.5% of the general population) without producing symptoms. It is often an isolated anomaly but may be associated with TOF with left arch, COA, or interrupted aortic arch. Its incidence is very high (38%) in Down syndrome with CHD.
- e. **Anomalous left PA (“vascular sling”)** is a rare anomaly in which the left PA arises from the right PA (Fig. 10-4). To reach the left lung, the anomalous artery courses over the proximal portion of the right main-stem bronchus, behind the trachea, and in front of the esophagus to the hilum of the left lung. Therefore, both respiratory symptoms and feeding problems (such as coughing, wheezing, stridor, and episodes of choking, cyanosis, or apnea) may occur. This anomaly is often associated with other CHDs, such as PDA, VSD, ASD, AV canal, or single ventricle.

Clinical Manifestations

1. Respiratory distress and feeding problems of varying severity appear at varying ages.
2. Physical examination reveals varying degrees of rhonchi. Cardiac examination is normal.
3. The ECGs are normal.
4. Chest radiographs may reveal compression of the air-filled trachea, aspiration pneumonia, or atelectasis. Barium esophagogram is usually diagnostic (see Fig. 10-4) except in anomalous innominate artery.
5. Echo is very helpful but limited for complete diagnosis of the vascular ring and associated intracardiac defects.

Diagnosis

1. **Barium esophagogram** is usually diagnostic of most vascular ring (see barium esophagograms in Fig. 10-4).
 - a. In double aortic arch, two large indentations are present in both sides (with the right one usually larger) in the posteroanterior (P-A) view, and a posterior indentation is seen on the lateral view.
 - b. In right aortic arch with left ligamentum arteriosum, a large right-sided indentation and a much smaller left-sided indentation are present. A posterior indentation, either small or large, also is present on the lateral view.
 - c. In anomalous left innominate artery, barium esophagogram is normal.
 - d. In aberrant right subclavian artery, a small oblique indentation extending toward the right shoulder on the P-A view and a small posterior indentation on the lateral view are present.
 - e. In vascular sling, an anterior indentation of the esophagus seen in the lateral view at the level of the carina is characteristic. This is the only vascular ring that produces an anterior esophageal indentation. A right-sided indentation usually is seen on the P-A view. The right lung is either hyperlucent or atelectatic with pneumonic infiltrations.

2. CT and MRI are often employed in the final diagnosis of the anomaly. They are very useful because they reveal not only the position of vascular structures but also of the tracheobronchial and esophageal structures and their relationships to the vascular structures. MRI has been proposed as an excellent substitute for angiography.
3. Occasionally, angiography is indicated to confirm the diagnosis

Management

Medical

1. Asymptomatic patients need no surgical treatment.
2. For infants with mild symptoms, careful feeding with soft foods and aggressive treatment of pulmonary infections are indicated.

Surgical

1. Indications and timing. Respiratory distress and a history of recurrent pneumonia and apneic spells are indications for surgical intervention.
2. Surgical procedures.
 - a. Double aortic arch. Division of the smaller of the two arches is performed. Knowing which arch is the dominant arch is very important, because thoracotomy is typically performed on the side of the smaller arch. The surgical mortality rate is <5%.
 - b. Right aortic arch and left ligamentum arteriosum. Ligation and division of the ligamentum is performed through a left thoracotomy. If a Kommerell diverticulum is found, the diverticulum is resected and the left subclavian artery is transferred to the left carotid artery. The mortality rate is <5%.
 - c. Anomalous innominate artery. Through right anterolateral thoracotomy, the innominate artery is suspended to the posterior sternum.
 - d. Aberrant right subclavian artery. The procedure consists of division of the aberrant artery and translocation to the right common carotid artery. It is performed only in symptomatic patients with dysphagia.
 - e. Anomalous left pulmonary artery. Surgical division and reimplantation of the left PA to the main PA is performed, usually through a median sternotomy and with the use of cardiopulmonary bypass.
3. Complications. In infants who have had surgery for severe symptoms, airway obstruction may persist for weeks or months after surgery. Careful respiratory management is required in the postoperative period.

ACQUIRED HEART DISEASES

In this part, cardiomyopathies, infective endocarditis, myocarditis, pericarditis, Kawasaki disease, acute rheumatic fever, valvular heart disease, cardiac tumors, and cardiac problems that may be associated with selected systemic diseases will be presented.

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Primary Myocardial Diseases (Cardiomyopathy)

Primary myocardial disease affects the heart muscle itself and is not associated with congenital, valvular, or coronary heart disease or systemic disorders. Cardiomyopathy has been classified into three types based on anatomic and functional features: (1) hypertrophic, (2) dilated (or congestive), and (3) restrictive (Fig. 11-1). Recently two new classifications have been added: arrhythmogenic cardiomyopathy and left ventricular non-compaction. Different subtypes of cardiomyopathy are functionally different from one another, and the demands of therapy are also different.

I. HYPERTROPHIC CARDIOMYOPATHY

In about 30% to 60% of cases, hypertrophic cardiomyopathy (HCM) appears to be genetically transmitted as an autosomal dominant trait, and in the remainder, it occurs sporadically. HCM is the most common cause of sudden cardiac death in teens and young adults, especially among athletes.

Pathology and Pathophysiology

1. A massive ventricular hypertrophy is present. Although asymmetric septal hypertrophy (ASH), formerly known as idiopathic hypertrophic subaortic stenosis (IHSS), is the most common type, a concentric hypertrophy with symmetric thickening of the LV sometimes occurs. Occasionally an intracavitary obstruction may develop during systole, partly because of systolic anterior motion (SAM) of the mitral valve against the hypertrophied septum, called hypertrophic obstructive cardiomyopathy (HOCM).
2. So-called apical hypertrophic cardiomyopathy is a variant of HCM in which hypertrophy is confined to the left ventricular apex, without intracavitary obstruction (and with giant negative T waves on the ECG). This subtype is present in about 25% of patients with HCM in Japan and less than 10% in other parts of the world.
3. The myocardium itself has an enhanced contractile state, but diastolic ventricular filling is impaired because of abnormal stiffness of the LV. This may lead to LA enlargement and pulmonary venous congestion, producing congestive symptoms (exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea).
4. About 80% of LV stroke volume occurs in the early part of systole when little or no obstruction exists, resulting in a sharp upstroke of arterial pulse.

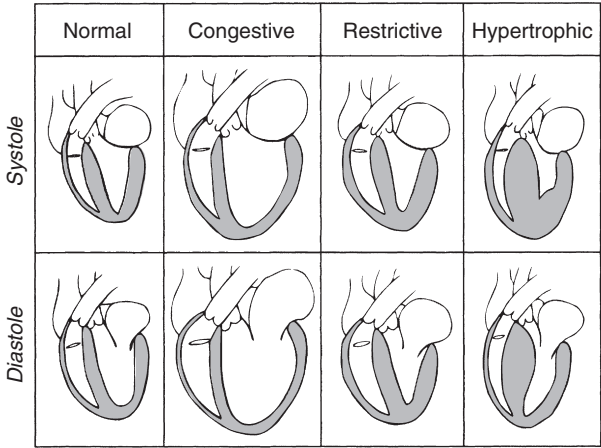


FIGURE 11-1
Diagram of left anterior oblique view of heart in different types of cardiomyopathy at end-systole and end-diastole. *Congestive* corresponds to *dilated* cardiomyopathy as used in the text. (From Goldman MR, Boucher CA: *Values of radionuclide imaging techniques in assessing cardiomyopathy*. Am J Cardiol 1980; 46: 1232-1236.)

5. A unique aspect of HOCM is the variability of the degree of obstruction from moment to moment.
 - a. The obstruction to LV output worsens when LV volume is reduced (as seen with positive inotropic agents, reduced blood volume, lowering of SVR, and so on).
 - b. The obstruction lessens when the LV systolic volume increases (negative inotropic agents, leg raising, blood transfusion, increasing SVR, and so on).
6. Anginal chest pain, syncope, and ventricular arrhythmias may lead to sudden death.
7. 10% to 20% of infants of diabetic mothers develop a transient form of HCM with or without LVOT obstruction. Children with LEOPARD syndrome commonly have HOCM (see Table 1-1).

Clinical Manifestations

1. Some 30% to 60% of cases are seen in adolescents and young adults with positive family history. Easy fatigability, dyspnea, palpitation, or anginal chest pain may be the presenting complaint.
2. A sharp upstroke of the arterial pulse is characteristic. A late systolic ejection murmur may be audible at the middle and lower LSB or at the apex. A holosystolic murmur (of MR) is occasionally present. The intensity and even the presence of the heart murmur vary from examination to examination in patients with HOCM.

3. The ECG may show LVH, ST-T changes, abnormally deep Q waves with diminished or absent R waves in the left precordial leads (LPLs), and arrhythmias. Occasionally “giant” negative T waves are seen in the LPLs in patients with apical hypertrophic cardiomyopathy.
4. Chest radiographs may show mild LV enlargement with globular heart.
5. Echo studies may demonstrate the following.
 - a. LV hypertrophy can be seen as concentric hypertrophy, localized segmental hypertrophy, asymmetrical septal hypertrophy (ASH), or localized to the apex.
 - b. ASH is present when the septal thickness is 1.4 times or greater than the posterior LV wall thickness.
 - c. In obstructive type, systolic anterior motion (SAM) of the mitral valve may be demonstrated. Doppler peak gradient in the LVOT of ≥ 30 mm Hg indicates an obstructive type.
 - d. In adults, LV diastolic wall thickness ≥ 15 mm (or on occasion, 13 or 14 mm), usually with LV dimension < 45 mm, is accepted as HCM. For children, z-score of 2 or more relative to BSA is compatible with the diagnosis.
 - e. Highly trained athletes may show LV hypertrophy, but the LV wall thickness ≥ 13 mm is very uncommon. In addition, it is always associated with an enlarged LV cavity (with LV diastolic dimension > 54 mm, with ranges of 55 to 63 mm). Therefore, trained adult athletes with LV wall thickness > 16 mm and a nondilated LV cavity are likely to have HCM.
 - f. The Doppler examination of the mitral inflow demonstrates signs of diastolic dysfunction with a decreased E velocity, an increased A velocity, and a decreased E/A ratio (usually < 0.8) (Fig. 11-2). These abnormalities are, however, nonspecific for HCM; they are also seen with dilated cardiomyopathy.
6. Natural history.
 - a. Obstruction may be absent, stable, or progressive (especially in genetically predisposed individuals).
 - b. Sudden death may occur during exercise, especially in those with episodes of ventricular tachycardia.
 - c. Atrial fibrillation may cause stroke.

Management

1. The goals of management are to (1) reduce LVOT obstruction (by reducing LV contractility and by increasing LV volume), (2) increase ventricular compliance, and (3) prevent sudden death (by preventing or treating ventricular arrhythmias). However, most therapeutic modalities used do not significantly reduce mortality rate.
2. General care.
 - a. Patients with HCM should avoid strenuous exercise or competitive sports, regardless of age, gender, symptoms, LVOT obstruction, or treatment.

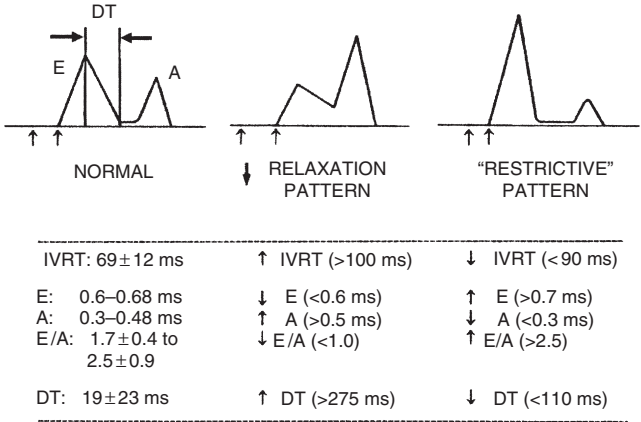


FIGURE 11-2
Examples of diastolic dysfunction seen in different types of cardiomyopathy. A, A wave (the velocity of a second wave that coincides with atrial contraction); DT, deceleration time (time from the peak of the E wave to the point where the decelerating diastolic velocity reaches the baseline); E, E wave (the velocity of an early peak that coincides with the early ventricular filling); E/A, ratio of E wave to A wave velocity; IVRT, isovolumic relaxation time (measured from the cessation of ventricular outflow to the onset of the E wave; between 2 small arrows). (Modified from Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

- b. First-degree relatives and other family members should be screened.
3. A β -adrenergic blocker (such as propranolol, atenolol, or metoprolol) or a calcium channel blocker (principally verapamil) is the drug of choice in the obstructive subgroup. These drugs reduce the degree of obstruction, decrease the incidence of anginal pain, and have antiarrhythmic actions.
 - a. A combination therapy with atenolol and verapamil may be considered in those patients with excessive LV hypertrophy and severe LVOT obstruction.
 - b. In small children, propranolol is the drug of choice due to liquid formulation and low side-effect profile. The dosage is 2 to 5 mg/kg/day given in 3 divided doses, with the heart rate goal of 80 to 100 beats per minute.
 - c. In older children, atenolol is typically used.
 - d. In infants of diabetic mothers, β -adrenergic blockers are used when the LVOT obstruction is present. In most of these infants, LV hypertrophy spontaneously resolves within the first 6 to 12 months of life.
4. Prophylactic therapy with either β -adrenergic blockers or verapamil is controversial in patients without LVOT obstruction. Some favor prophylactic use of these drugs even in the absence of LVOT

obstruction; others limit prophylactic drug therapy to young patients with a family history of premature sudden death and those with particularly marked LVH.

5. The following drugs are contraindicated: digitalis, other inotropic agents, and vasodilators tend to increase LVOT obstruction; diuretics may reduce LV volume and increase LVOT obstruction (but may be used in small doses to improve respiratory symptoms).
6. Morrow's myotomy-myectomy or percutaneous alcohol ablation may be considered for drug-refractory patients with LVOT obstruction.
 - a. In Morrow's procedure, hypertrophied LV septum is resected through a transaortic approach to reduce the obstruction.
 - b. In alcohol ablation, absolute alcohol is injected into a target septal perforator branch of the left anterior descending coronary artery to produce "controlled" MI.
7. Implantable cardioverter defibrillator (ICD) has been proved to be effective in preventing sudden death. The following are risk factors for sudden death in HCM and may be indications for an ICD.
 - a. Prior cardiac arrest (ventricular fibrillation)
 - b. Spontaneous sustained ventricular tachycardia (defined as 3 or more beats at ≥ 120 beats/min on Holter ECG)
 - c. Family history of premature sudden death
 - d. Unexplained syncope, particularly in young patients
 - e. LV thickness ≥ 30 mm, particularly in adolescents and young adults
 - f. Nonsustained VT
 - g. Abnormal exercise BP (attenuated response or hypotension)
8. Cardiac arrhythmias.
 - a. Ventricular arrhythmias are treated with propranolol, amiodarone, and other antiarrhythmic agents, guided by serial ambulatory ECG monitoring.
 - b. Atrial fibrillation (AF) occurs more often in patients with LA enlargement. For a new onset AF, electrical cardioversion followed by anticoagulation with warfarin (superior to aspirin) is recommended. Amiodarone is generally considered as the most effective agent for preventing recurrence of AF.

II. DILATED (CONGESTIVE) CARDIOMYOPATHY

Causes

1. Dilated cardiomyopathy (DCM) is the most common form of cardiomyopathy. The cause of the condition is idiopathic in about 50% of the cases. Among the known causes of DCM are myocarditis (46%) and neuromuscular diseases ($\approx 25\%$), followed by familial cardiomyopathy, active myocarditis, and others. Some cases of idiopathic dilated cardiomyopathy may be the result of subclinical myocarditis.
2. Some of the patients with idiopathic DCM may have tachycardia-induced cardiomyopathy, which is related to chronic tachycardia (usually atrial or supraventricular tachycardia).

3. Other rare causes of DCM include infectious causes other than viral infection (bacterial, fungal, protozoan, rickettsial), endocrine-metabolic disorders (hyper- and hypothyroidism, excessive catecholamines, diabetes, hypocalcemia, hypophosphatemia, glycogen storage disease, mucopolysaccharidoses), and nutritional disorders (kwashiorkor, beriberi, carnitine deficiency).
4. Cardiotoxic agents such as doxorubicin and systemic diseases (such as connective tissue diseases) can also cause dilated cardiomyopathy.

Pathology and Pathophysiology

1. In DCM, a weakening of systolic contraction is associated with dilatation of all four cardiac chambers. Dilatation of the atria is in proportion to ventricular dilatation.
2. Intracavitary thrombus formation is common in the apical portion of the ventricular cavities and in atrial appendages, and it may give rise to pulmonary and systemic embolization.

Clinical Manifestations

1. Fatigue, weakness, and symptoms of left heart failure (e.g., dyspnea on exertion, orthopnea) may be present.
2. On physical examination, signs of CHF (e.g., tachycardia, pulmonary crackles, weak pulses, distended neck veins, hepatomegaly) may be present. A prominent S3 with or without gallop rhythm is present. A soft systolic murmur of MR or TR may be audible.
3. The ECG commonly shows sinus tachycardia, LVH, and ST-T changes.
4. Chest radiographs show generalized cardiomegaly, often with signs of pulmonary venous congestion.
5. Echo studies are diagnostic and may include unexpected findings in an asymptomatic patient.
 - a. The LV and RV are markedly dilated with poor contractility. The LA may be enlarged.
 - b. Fractional shortening (FS) and ejection fraction (EF) are reduced.
 - c. Intracavitary thrombus and pericardial effusion may be present.
 - d. The mitral inflow Doppler tracing demonstrates a reduced E velocity and a decreased E/A ratio: nonspecific signs (see [Fig. 11-2](#)).
6. Although echo study is diagnostic, cardiac catheterization can be helpful (1) to exclude anomalous coronary artery, (2) to predict etiology and prognosis by obtaining endomyocardial biopsy, and (3) to evaluate for possible cardiac transplantation including measurement of pulmonary vascular resistance.
7. Progressive deterioration is the rule rather than the exception for many patients. Cardiac arrhythmias, systemic or pulmonary embolization, and CHF are common causes of death. However, a recent review of literature in children suggests approximately one third die, one third recover completely, and one third improve with some residual cardiac dysfunction.

Management

1. CHF is treated with digoxin, diuretics (furosemide, spironolactone), ACE inhibitors (captopril, enalapril), bed rest, and restriction of activity. Critically ill patients may require intubation, mechanical ventilation, and administration of rapidly acting inotropic agents (dobutamine, dopamine).
2. Antiplatelet agents (aspirin) should be initiated. Anticoagulation with warfarin may be indicated. If thrombi are detected they should be treated aggressively with heparin initially and later switched to long-term warfarin therapy.
3. Patients with arrhythmias may be treated with amiodarone or other antiarrhythmic agents. Amiodarone is effective and relatively safe in children. For symptomatic bradycardia, a cardiac pacemaker may be necessary. An implantable cardioverter-defibrillator (ICD) may be considered.
4. The beneficial effects of β -adrenergic blocking agents (somewhat unorthodox, given poor contractility) have been reported in adult and pediatric patients. Recent evidence suggests that activation of the sympathetic nervous system may have deleterious cardiac effects on failing hearts (rather than being an important compensatory mechanism, as traditionally thought). β -Adrenergic blockers may exert beneficial effects by a negative chronotropic effect with reduced oxygen demand, reduction in catecholamine toxicity, inhibition of sympathetically mediated vasoconstriction, or reduction of potentially lethal ventricular arrhythmias. Among β -adrenergic blockers, carvedilol is preferable because of the additional vasodilating action of the drug.
5. If carnitine deficiency is considered as the cause for the cardiomyopathy, carnitine supplementation should be started.
6. A preliminary report suggests that administration of recombinant human growth hormone (0.025-0.04 mg/kg/day for 6 months) may improve LV ejection fraction, increase LV wall thickness, reduce the chamber size, and improve cardiac output.
7. The utility of immunosuppressive agents, including steroids, cyclosporine, and azathioprine, remains unproved.
8. Many of these children may become candidates for cardiac transplantation.

III. DOXORUBICIN CARDIOMYOPATHY

Etiology and Pathology

1. Doxorubicin cardiomyopathy is becoming one of the most common causes of chronic CHF in children. Its prevalence is nonlinearly dose related, occurring in 2% to 5% of patients who have received a cumulative dose of 400 to 500 mg/m² and up to 50% of patients who have received more than 1000 mg/m² of doxorubicin (Adriamycin).
2. Risk factors for developing doxorubicin cardiomyopathy include the following.

- a. Patients who received cumulative dose of anthracyclines $> 360 \text{ mg/m}^2$. They are 40 times more likely to die than those who received $< 240 \text{ mg/m}^2$.
 - b. Age younger than 4 years.
 - c. Concomitant cardiac irradiation.
 - d. A dosing regimen with larger and less frequent doses has been raised as a risk factor but not proved.
3. Dilated LV, decreased contractility, and elevated LV filling pressure are present.

Clinical Manifestations

1. Patients have a history of receiving doxorubicin, with the onset of symptoms 2 to 4 months, and rarely years, after completion of therapy.
2. Patients are usually asymptomatic until signs of CHF develop. Tachypnea and exertional dyspnea are the usual presenting complaints. Signs of CHF may be present on physical examination.
3. Chest radiographs show cardiomegaly with or without pulmonary congestion or pleural effusion.
4. The ECG frequently shows sinus tachycardia with occasional ST-T changes. During doxorubicin therapy, a prolonged QTc interval occurs in 40% of patients immediately after a single dose.
5. Echo abnormalities of DCM are present, including slightly increased LV size, reduced LV wall thickness, and decreased ejection fraction or fractional shortening. During doxorubicin therapy, echo may show reduced ejection fraction or fractional shortening (but stopping therapy based on these changes may not be justified).
6. Symptomatic patients have a high mortality rate. The 2-year survival rate is about 20%, and almost all patients die by 9 years after the onset of the illness.

Management

1. Attempts to reduce anthracycline cardiotoxicity have been made in four directions: (1) anthracycline dose limitation; (2) method of drug administration; (3) developing less cardiotoxic analogs; and (4) concurrently administering cardioprotective agents to attenuate the cardiotoxic effects of anthracycline to the heart.
 - a. Limiting the total cumulative dose to 400 to 500 mg/m^2 reduces the incidence of CHF to 5%, but this dose may not be effective in treating some malignancies.
 - b. Continuous infusion therapy may reduce cardiac injury by avoiding peak levels, but a recent study reports no cardioprotection of continuous infusion.
 - c. Analogs of doxorubicin such as idarubicin and epirubicin have not been proved to be less toxic than doxorubicin.
 - d. Concurrent administration of the cardioprotective agents such as dexrazoxane (an iron chelator), carvedilol (a β -receptor antagonist with

antioxidant property), and coenzyme Q10 have shown some protective effects, without attenuating the antimalignancy effect of the drug.

Among these, dexrazoxane appears to be most cardioprotective.

2. Unfortunately, no effective treatment for established doxorubicin cardiomyopathy is presently available. Currently, the following medications are used.
 - a. Digoxin, diuretics, and ACE inhibitors are useful.
 - b. β -blockers have been shown to be beneficial in some children and adults with chemotherapy-induced cardiomyopathy.
 - (1) Metoprolol (starting at 0.1 mg/kg per dose twice a day and increasing to a maximum dose of 0.9 mg/kg per day) has improved LV systolic function and improved symptoms.
 - (2) Carvedilol with additional vasodilator and antioxidant effects (12.5 mg once daily) given for 6 months to patients concurrently receiving Adriamycin was shown to prevent ventricular dilatation and maintain their ejection fraction at approximately 70%.
3. Cardiac transplantation may be an option for selected patients.

IV. CARNITINE DEFICIENCY

Carnitine deficiency is a rare cause of cardiomegaly in infants and small children. Carnitine deficiency leads to depressed mitochondrial oxidation of fatty acids, resulting in storage of fat in muscles and in functional abnormalities of cardiac and skeletal muscles. Carnitine is synthesized predominantly in the liver.

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A. Primary Carnitine Deficiency

Primary carnitine deficiency is an uncommon inherited disorder. The condition has been classified as either systemic or myopathic.

1. The *systemic form* of the disease may manifest with muscle weakness, cardiomyopathy (either hypertrophic or dilated), abnormal liver function, encephalopathy, and hypoglycemia during fasting in the first year of life. Low concentrations of carnitine are present in plasma, muscle, and liver.
2. In the *myopathic form*, progressive cardiomyopathy is the most common manifestation, with or without skeletal muscle weakness that begins at 2 to 4 years of age. Biopsy reveals fatty infiltration of muscle fibers. The ECG may show bizarre T wave spiking. Those affected die suddenly, presumably from arrhythmias.

B. Secondary Forms of Carnitine Deficiency

Secondary carnitine deficiency has been reported in renal tubular disorders (with excessive excretion of carnitine), chronic renal failure (excessive loss of carnitine from hemodialysis), inborn errors of metabolism with increased concentrations of organic acids, and occasional patients who receive total parenteral nutrition. Diagnosis of the condition is established by an extremely low level of carnitine in plasma and skeletal muscle.

Treatment

For both forms, oral carnitine (L-carnitine: 50–100 mg/kg/day, BID or TID; maximum daily dose 3 g) may improve myocardial function, reduce cardiomegaly, and improve muscle weakness.

V. RESTRICTIVE CARDIOMYOPATHY

Prevalence and Causes

1. Restrictive cardiomyopathy is an extremely rare form of cardiomyopathy, accounting for 5% of cardiomyopathy cases in children.
2. It may be idiopathic, or it may be associated with a systemic infiltrative disease (such as scleroderma, amyloidosis, and sarcoidosis) or an inborn error of metabolism (mucopolysaccharidosis). Malignancies or radiation therapy may result in restrictive cardiomyopathy.

Pathology and Pathophysiology

1. The condition is characterized by an abnormal ventricular diastolic filling owing to excessively stiff ventricular walls.
2. The ventricles are normal in size and in systolic function. Only the atria are markedly dilated, a characteristic finding of the condition.
3. There are areas of myocardial fibrosis and hypertrophy of myocytes, or the myocardium may be infiltrated by various materials.

Clinical Manifestations

1. History of exercise intolerance, weakness and dyspnea, or chest pain may be present.
2. Jugular venous distention, hepatomegaly, a loud S2 (P2), gallop rhythm, and a systolic murmur of MR or TR may be present.
3. Chest radiographs show cardiomegaly, pulmonary congestion, and pleural effusion.
4. The ECG usually shows RAH and/or LAH. It may show atrial fibrillation and paroxysms of SVT.
5. Echo studies reveal the following:
 - a. Characteristic biatrial enlargement with normal dimensions of the LV and RV.
 - b. Normal LV systolic function (ejection fraction) until the late stages of the disease.
 - c. Abnormal diastolic function (with increased E velocity and increased E/A ratio, and shortened deceleration time (see [Fig. 11-2](#)).
 - d. Possible atrial thrombus.
6. Differentiation of restrictive cardiomyopathy from *constrictive pericarditis* is important because the latter can be treated successfully with pericardiectomy.
 - a. In constrictive pericarditis, echo shows a thickened pericardium and Doppler studies show a marked respiratory variation in the filling phase, although both conditions show similar Doppler findings of diastolic dysfunction.

- b. Cardiac catheterization shows similar hemodynamic data in both conditions, although pulmonary hypertension is worse in restrictive cardiomyopathy.
- c. Endomyocardial biopsy reveals myocyte hypertrophy and interstitial fibrosis; it may also reveal a specific cause.
- d. Rarely, surgical exploration may be needed.

Management

Treatment is directed at alleviating symptoms. In general, medical therapy does not improve survival. The prognosis is poor.

1. Diuretics are beneficial by relieving congestive symptoms.
2. Calcium channel blockers may be used to increase diastolic compliance.
3. Digoxin is not indicated, because systolic function is unimpaired.
4. ACE inhibitors should not be used because they may reduce systemic BP without increasing cardiac output.
5. Anticoagulants (warfarin) and antiplatelet drugs (aspirin and dipyridamole) may help prevent thrombosis.
6. Permanent pacemaker is indicated for complete heart block.
7. Cardiac transplantation may be an option before pulmonary hypertension develops.

VI. ARRHYTHMOGENIC CARDIOMYOPATHY (ARRHYTHMOGENIC RV DYSPLASIA, RV DYSPLASIA, OR RV CARDIOMYOPATHY)

11

Prevalence and Pathology

1. This rare anomaly of unknown etiology is more prevalent in northern Italy.
2. The myocardium of the RV is partially or totally replaced by fibrous or adipose tissue. The RV wall may rarely assume a paper-thin appearance. The LV is usually spared.

Clinical Manifestations

1. The onset is in infancy, childhood, or adulthood (but usually before age 20 years), with history of palpitation, syncopal episodes, or both. It accounts for about 5% of sudden cardiac death.
2. Presenting manifestations may be arrhythmias (VT, SVT) or signs of CHF.
3. The ECG often shows tall P waves in lead II (RAH), decreased RV forces, T wave inversion in the right precordial leads (nonspecific; normal in children), RBBB, and PVCs or VT of LBBB morphology.
4. Chest radiographs usually show cardiomegaly.
5. Echo studies show selective RV enlargement, extreme thinning of the RV free wall, often with systolic bulging, the hallmark of the condition.
6. Cardiac MRI and RV angiogram show similar findings as echo studies. Endomyocardial biopsy obtained from the septum may not show the characteristic histologic changes (with high false negative results).
7. A substantial portion of patients die before 5 years of age from CHF and intractable ventricular tachycardia.

Management

1. Various antiarrhythmic agents are often unsuccessful in abolishing ventricular arrhythmias.
2. Surgical intervention (ventricular incision or complete electrical disarticulation of the RV free wall) may be tried if antiarrhythmic therapy is unsuccessful.
3. ICD may be indicated in selected patients.

VII. NONCOMPACTION CARDIOMYOPATHY (LEFT VENTRICULAR NONCOMPACTION, LEFT VENTRICULAR HYPERTRABECULATION)

Cause

This condition results from an intrauterine arrest of normal compaction of the loose interwoven meshwork of the ventricular myocardium (which normally occurs during the first month of fetal life). Mutations in the gene G4.5 on the Xq28 may be responsible for noncompaction. Familial occurrence has been reported in up to 25%.

Clinical Manifestations

1. Most of the patients with this disorder are asymptomatic.
2. Cardiac examination may be entirely normal. Signs of LV dysfunction may be present or eventually develop.
3. Nearly 30% of the patients have neurologic disorders including seizures, hypotonia, myopathy, or mental/motor retardation.
4. The ECG may show giant QRS complexes, sometimes with WPW preexcitation.
5. Chest radiographs are usually normal.
6. Echo findings:
 - a. Characteristic echo findings are segmental thickening of the LV wall consisting of 2 layers with a thin compacted epicardial layer and an extremely thickened noncompacted endocardial layer with prominent trabeculations and deep recesses. Apical and midventricular segments of both the inferior and lateral walls are most commonly affected.
 - b. LV systolic dysfunction is seen in 35% to 90% of pediatric patients. LV diastolic dysfunction is often present.
7. Heart failure usually worsens despite optimal treatment. Arrhythmias and thromboembolic events are mostly seen in adults, but they may also be seen in children.

Treatment

1. Anticongestive measures with digoxin, diuretic, and afterload reducing agents are usually used. The use of carvedilol, a β -blocker, should be considered in patients with LV dysfunction; it has been shown to improve LV dysfunction.
2. All patients should be on an antiplatelet dose of aspirin. If thrombosis is detected, anticoagulation with Coumadin should be started.

3. Appropriate antiarrhythmic therapy is indicated. Implantation of ICD may be considered for life-threatening ventricular arrhythmias.
4. Patients with dysmorphic features or neurologic manifestations may need detailed metabolic screening (for example, fatty acid oxidation disorder or mitochondrial disease).
5. Heart transplantation is a possible option for selected patients.

Chapter 12

Cardiovascular Infections and Related Conditions

I. INFECTIVE ENDOCARDITIS (SUBACUTE BACTERIAL ENDOCARDITIS)

Prevalence

Subacute bacterial endocarditis (SBE) affects 0.5:1000 to 1:1000 hospital patients, excluding those with postoperative endocarditis.

Pathology and Pathogenesis

1. Two factors are important in the pathogenesis of infective endocarditis (IE): (1) structural abnormalities of the heart or great arteries with a significant pressure gradient or turbulence, with resulting endothelial damage and platelet-fibrin thrombus formation, and (2) bacteremia, even if transient, with adherence of the organisms and eventual invasion of the underlying tissue.
2. Those with a prosthetic heart valve or prosthetic material in the heart are at particularly high risk for IE because these promote deposition of sterile thrombus.
3. Almost all patients who develop IE have a history of congenital or acquired heart disease. Drug addicts may develop endocarditis in the absence of known cardiac anomalies.

Microbiology

1. In the past, *Streptococcus viridans*, enterococci, and *Staphylococcus aureus* were responsible for over 90% of cases of IE. In recent years, this frequency has decreased to 50% to 60%, with a concomitant increase in cases caused by fungus and HACEK organisms (*Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, and *Kingella*).
2. Alpha-hemolytic streptococci (*S. viridans*) are the most common cause of IE following dental procedures or in those patients with carious teeth or periodontal disease.
3. Enterococci are the organisms most often found after genitourinary or gastrointestinal surgery or instrumentation.
4. The organisms most commonly found in postoperative endocarditis are staphylococci.

Clinical Manifestations

1. Most patients are known to have an underlying heart disease. The onset is usually insidious with prolonged low-grade fever (101° F and 103° F) and various somatic complaints.

2. Heart murmur is almost always present and splenomegaly is common (70%).
3. Skin manifestations (50%) may be present in the following forms:
 - a. Petechiae on the skin, mucous membranes, or conjunctivae are frequent.
 - b. Osler nodes (tender, pea-sized red nodes at the ends of the fingers or toes) are rare in children.
 - c. Janeway lesions (small, painless, hemorrhagic areas on the palms or soles) are rare.
 - d. Splinter hemorrhages (linear hemorrhagic streaks beneath the nails) also are rare.
4. Embolic or immunologic phenomena in other organs are present in 50% of cases.
 - a. Pulmonary emboli or hematuria and renal failure may occur.
 - b. Seizures and hemiparesis (20%) may occur.
 - c. Roth spots (oval, retinal hemorrhages with pale centers located near the optic disc) occur in <5% of patients.
5. Laboratory studies.
 - a. Positive blood cultures are obtained in more than 90% of patients in the absence of previous antimicrobial therapy.
 - b. Anemia and leukocytosis with a shift to the left are common.
 - c. The sedimentation rate is increased unless there is polycythemia.
 - d. Microscopic hematuria is found in 30% of patients.
6. Echocardiography. Although standard transthoracic echo (TTE) is sufficient in most cases, transesophageal echo (TEE) may be needed in obese or very muscular adolescents.
 - a. The following echo findings are included as major criteria in the modified Duke criteria: (1) oscillating intracardiac mass on valve or supporting structures, in the path of regurgitation jets or on implanted material; (2) abscesses; (3) new partial dehiscence of prosthetic valve; and (4) new valvular regurgitation.
 - b. The absence of vegetations on echo does not in itself rule out IE. False negative diagnosis is possible if vegetations are small or have already embolized.
 - c. Conversely, a false positive diagnosis is possible. An echogenic mass may represent a sterile thrombus, sterile prosthetic material, normal anatomic variation, an abnormal uninfected valve (previous scarring, severe myxomatous changes), or improper gain of the echo machine. Echo evidence of vegetation may persist for months or years after bacteriologic cure.
 - d. Certain echo features suggest a high-risk case or a need for surgery: (1) large vegetations (greatest risk when the vegetation is >10 mm), (2) severe valvular regurgitation, (3) abscess cavities, (4) pseudoaneurysm, or (5) valvular perforation or dehiscence.

Diagnosis

The diagnosis of infective endocarditis is challenging. The modified Duke criteria are used in the diagnosis. There are three categories of diagnostic

BOX 12-1

DEFINITION OF INFECTIVE ENDOCARDITIS ACCORDING TO THE MODIFIED DUKE CRITERIA

DEFINITE IE

- A. Pathological criteria
 - 1. Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
 - 2. Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis
- B. Clinical criteria
 - 1. 2 major criteria; or
 - 2. 1 major criterion and 3 minor criteria; or
 - 3. 5 minor criteria

POSSIBLE IE

- 1. 1 major criterion and 1 minor criterion; or
- 2. 3 minor criteria

REJECTED

- 1. Firm alternative diagnosis explaining evidence of IE; or
- 2. Resolution of IE syndrome with antibiotic therapy for <4 days; or
- 3. No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for <4 days; or
- 4. Does not meet criteria for possible IE as above

From Baddour LM, Wilson WR, Bayer AS et al: Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association, *Circulation*. 111(23):e394-e433, 2005.

possibilities using the modified Duke criteria: definite, possible, and rejected. A diagnosis of “definite” IE is made either by pathologic evidence or fulfillment of certain clinical criteria (see [Box 12-1](#)). [Box 12-2](#) shows definitions of major and minor clinical criteria.

Management

- 1. Blood cultures are indicated for all patients with fever of unexplained origin and a pathologic heart murmur, a history of heart disease, or previous endocarditis.
 - a. Usually three blood cultures are drawn over 24 hours, unless the patient is very ill. In 90% of cases, the causative agent is recovered from the first two cultures.
 - b. If there is no growth by the second day of incubation, two more cultures may be obtained. There is no value in obtaining more than five blood cultures over 2 days unless the patient received prior antibiotic therapy.

BOX 12-2

DEFINITION OF MAJOR AND MINOR CLINICAL CRITERIA FOR THE DIAGNOSIS OF INFECTIVE ENDOCARDITIS**MAJOR CRITERIA**

- A. Blood culture positive for IE
1. Typical microorganisms consistent with IE from 2 separate blood cultures: Viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*; or community-acquired enterococci in the absence of a primary focus; or
 2. Microorganisms consistent with IE from persistently positive blood cultures defined as follows: At least 2 positive cultures of blood samples drawn >12 hr apart; or all of 3 or a majority of ≥ 4 separate cultures of blood (with first and last sample drawn at least 1 hr apart)
 3. Single positive blood culture for *Coxiella burnetii* or anti-phase 1 IgG antibody titer >1:800
- B. Evidence of endocardial involvement
- Echocardiogram positive for IE (transesophageal echo [TEE] recommended for patients with prosthetic valves, rated at least “possible IE” by clinical criteria, or complicated IE [paravalvular abscess]; transthoracic echo (TTE) as first test in other patients) defined as follows:
1. Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or
 2. Abscess; or
 3. New partial dehiscence of prosthetic valve; or
 4. New valvular regurgitation (worsening or changing or preexisting murmur not sufficient)

MINOR CRITERIA

1. Predisposition, predisposing heart condition, or injection drug users
2. Fever, temperature $>38^{\circ}\text{C}$
3. Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions
4. Immunologic phenomena: glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor
5. Microbiologic evidence: positive blood culture but does not meet a major criterion as noted above* or serologic evidence of active infection with organism consistent with IE

*Excludes single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis.

From Baddour LM, Wilson WR, Bayer AS et al: Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association, *Circulation*. 111(23):e394-e433, 2005.

- c. Aerobic incubation alone suffices because it is rare for IE to be due to anaerobic bacteria.
2. Initial empirical therapy is started with the following antibiotics while awaiting the results of blood cultures. Consultation from a local infectious disease specialist is strongly recommended.
 - a. The usual initial regimen is an antistaphylococcal semisynthetic penicillin (nafcillin, oxacillin, or methicillin) and an aminoglycoside (gentamicin). This combination covers against *S. viridans*, *S. aureus*, and gram-negative organisms.
 - b. If a methicillin-resistant *S. aureus* is suspected, vancomycin should be substituted for the semisynthetic penicillin.
 - c. Vancomycin can be used in place of penicillin or a semisynthetic penicillin in penicillin-allergic patients.
3. The final selection of antibiotics for native valve IE depends on the organism isolated and the results of an antibiotic sensitivity test.
 - a. Streptococcal infective endocarditis
 - (1) For highly sensitive *S. viridans*, IV penicillin (or ceftriaxone given once daily) for 4 weeks is sufficient. Alternatively, penicillin, ampicillin, or ceftriaxone combined with gentamicin for 2 weeks may be used.
 - (2) For penicillin-resistant streptococci, 4 weeks of penicillin, ampicillin, or ceftriaxone combined with gentamicin for the first 2 weeks is recommended.
 - b. Staphylococcal endocarditis
 - (1) For methicillin-susceptible staphylococci IE, one of the semi-synthetic β -lactamase-resistant penicillins (nafcillin, oxacillin, or methicillin) for a minimum of 6 weeks (with or without gentamicin for the first 3-5 days) is used.
 - (2) For patients with methicillin-resistant IE, vancomycin for 6 weeks (with or without gentamicin for the first 3-5 days) is used.
 - c. Enterococcus-caused endocarditis usually requires a combination of IV penicillin or ampicillin together with gentamicin for 4 to 6 weeks. If patients are allergic to penicillin, vancomycin combined with gentamicin for 6 weeks is required.
 - d. For HACEK organisms, ceftriaxone or another third-generation cephalosporin alone or ampicillin plus gentamicin for 4 weeks is recommended. IE caused by other gram-negative bacteria (such as *E. coli*, *Pseudomonas aeruginosa*, or *Serratia marcescens*) is treated with piperacillin or ceftazidime together with gentamicin for a minimum of 6 weeks.
 - e. For fungal IE, amphotericin B is the most effective agent.
 - f. In culture-negative endocarditis, treatment is directed against staphylococci, streptococci, and the HACEK organisms using ceftriaxone and gentamicin. When staphylococcal IE is suspected, nafcillin should be added to the above therapy.
4. Patients with prosthetic valve endocarditis should be treated for 6 weeks based on the organism isolated and the results of the sensitivity test.

Operative intervention may be necessary before the antibiotic therapy is completed if the clinical situation warrants (such as progressive CHF, significant malfunction of prosthetic valves, persistently positive blood cultures after 2 weeks' therapy). Bacteriologic relapse after an appropriate course of therapy also calls for operative intervention.

Prognosis

The overall recovery rate is 80% to 85%; it is 90% or better for *S. viridans* and enterococci, and about 50% for *Staphylococcus* organisms. Fungal endocarditis is associated with a very poor outcome.

Prevention

1. The following are recommendations for antibiotic prophylaxis according to the American Heart Association (2007).
 - a. Antibiotic prophylaxis is recommended only for cardiac conditions listed in [Box 12-3](#).
 - b. Procedures for which antibiotic prophylaxis is recommended and those not recommended are listed in [Box 12-4](#).
 - c. Antibiotic choices and dosages for dental procedures are shown in [Table 12-1](#).
2. Special situations.
 - a. For patients who are on rheumatic fever prophylaxis, use other antibiotics, such as clindamycin, azithromycin, or clarithromycin, rather than using a higher dose of the same antibiotic.
 - b. When the patient is already on a course of an antibiotic for other reasons (such as tonsillitis), delay a dental procedure, if possible, until at least 10 days after completion of the antibiotic therapy.

BOX 12-3

CARDIAC CONDITIONS FOR WHICH PROPHYLAXIS WITH DENTAL PROCEDURES IS RECOMMENDED

1. Prosthetic cardiac valve
2. Previous infective endocarditis
3. Congenital heart disease (CHD)*:
 - a. Unrepaired cyanotic CHD, including palliative shunts and conduits
 - b. Completely repaired CHD with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure§
 - c. Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibits endothelialization)
4. Cardiac transplantation recipients who develop cardiac valvulopathy

*Except for conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of CHD.

§Prophylaxis is recommended because endothelialization of prosthetic material occurs within 6 months after the procedure.

BOX 12-4

PROCEDURES FOR WHICH ENDOCARDITIS PROPHYLAXIS IS RECOMMENDED

1. Dental procedures
All dental procedures that involve manipulation of gingival tissue of the periapical region of teeth or perforation of the oral mucosa. Antibiotic choices and dosages for dental procedures are shown in [Table 12-1](#).
2. Respiratory tract procedures
 - a. Recommended for procedures that involve incision or biopsy of the respiratory mucosa, such as tonsillectomy and adenoidectomy
 - b. Not recommended for bronchoscopy (unless it involves incision of the mucosa, such as for abscess or empyema)
3. Gastrointestinal (GI) and genitourinary (GU) procedures
 - a. No prophylaxis for diagnostic esophagogastroduodenoscopy or colonoscopy
 - b. Prophylaxis is reasonable in patients with infected GI or GU tract (with amoxicillin or ampicillin to cover against enterococci)
4. Skin, skin structure, or musculoskeletal tissue
 - a. Recommended for surgical procedures that involve infected skin, skin structure, or musculoskeletal tissue (with antibiotics against staphylococcus and β -hemolytic streptococcus, such as antistaphylococcal penicillin or a cephalosporin)
 - b. Vancomycin or clindamycin is administered if unable to tolerate β -lactam or if infection is caused by methicillin-resistant staphylococcus

TABLE 12-1

PROPHYLACTIC REGIMENS FOR DENTAL PROCEDURES

SITUATION	AGENT	Single dose 30-60 min before procedure	
		CHILDREN	ADULTS
Oral	Amoxicillin	50 mg/kg	2 g
Unable to take oral medications	Ampicillin, or	50 mg/kg (IM, IV)	2 g (IM, IV)
	Cefazolin or ceftriaxone	50 mg/kg (IM, IV)	1 g (IM, IV)
Allergic to penicillin or ampicillin—oral	Cephalexin *† or	50 mg/kg	2 g
	Clindamycin, or	20 mg/kg	600 mg
	Azithromycin or clari- thromycin	15 mg/kg	500 mg
Allergic to penicillin or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone	50 mg/kg (IM, IV)	1 g (IM, IV)
	Clindamycin	20 mg/kg	600 mg

*Or other first- or second-generation oral cephalosporin in equivalent adult or pediatric dosage.

†Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillin or ampicillin.

3. For patients who undergo cardiac surgery, the following applies:
 - a. A careful preoperative dental evaluation is recommended so that required dental treatment may be completed before cardiac surgery.
 - b. Prophylaxis at the time of surgery should be directed primarily against staphylococci and should be of short duration.

- c. Prophylaxis should be initiated immediately before the operative procedure, repeated during prolonged procedures to maintain serum concentrations intraoperatively, and continued for no more than 48 hours postoperatively.

II. MYOCARDITIS

Prevalence

Myocarditis severe enough to be recognized clinically is rare, but the prevalence of mild and subclinical cases is probably much higher.

Etiology

1. Infections: Viruses (such as adenovirus, coxsackieviruses, echoviruses, and many others) are the most common cause of myocarditis in North America. In South America, Chagas disease (caused by *Trypanosoma cruzi*, a protozoan) is far more common. Rarely, bacteria, rickettsia, fungi, protozoa, and parasites are the causative agents.
2. Immune-mediated diseases: acute rheumatic fever, Kawasaki disease.
3. Collagen vascular diseases.
4. Toxic myocarditis (drug ingestion, diphtheria exotoxin, and anoxic agents).

Pathology

1. The principal mechanism of cardiac involvement in viral myocarditis is believed to be a cell-mediated immunologic reaction, not merely myocardial damage from viral replication. Isolation of virus from the myocardium is unusual at autopsy.
2. Microscopic examination reveals patchy infiltrations by plasma cells, mononuclear leukocytes, and some eosinophils during the acute phase and giant cell infiltration in the later stages.

Clinical Manifestations

1. History of an upper respiratory infection may be present in older children. The onset of illness may be sudden in neonates and small infants, causing anorexia, vomiting, lethargy, and occasionally circulatory shock. In older children, a gradual onset of CHF and arrhythmia are commonly seen.
2. A soft, systolic ejection murmur and irregular rhythm caused by supra-ventricular or ventricular ectopic beats may be audible. Hepatomegaly (evidence of viral hepatitis) may be present.
3. The ECG may show any one or a combination of the following: low QRS voltages, ST-T changes, prolongation of the QT interval, and arrhythmias, especially premature contractions.
4. Cardiomegaly on chest radiograph is the most important clinical sign of myocarditis.
5. Echo studies reveal cardiac chamber enlargement and impaired LV systolic function. Occasionally, LV thrombi are found.

6. Cardiac troponin (I and T) levels and myocardial enzymes (creatine kinase [CK], MB isoenzyme of CK [CK-MB]) may be elevated. Troponin levels may be more sensitive than the cardiac enzymes. The normal value of cardiac troponin I in children is 2.0 ng/mL or less.
7. Radionuclide scanning (after administration of gallium-67 or technetium-99m pyrophosphate) may identify inflammatory and necrotic changes characteristic of myocarditis. Myocarditis can be confirmed by an endomyocardial biopsy.
8. The mortality rate is as high as 75% in symptomatic neonates with acute viral myocarditis. In children, the majority of patients, especially those with mild inflammation, recover completely. Some patients develop sub-acute or chronic myocarditis with persistent cardiomegaly with or without signs of CHF and ECG evidence of LVH or BVH. Clinically, these patients are indistinguishable from those with dilated cardiomyopathy. Myocarditis may be a precursor to some cases of idiopathic dilated cardiomyopathy.

Management

1. Virus identification by viral cultures from the blood, stool, or throat washing should be attempted, and comparison of acute and convalescent sera may be made for serologic titer rise.
2. Bed rest and limitation of activities are recommended during the acute phase.
3. Beneficial effects of high-dose γ -globulin (2 g/kg over 24 hours) have been reported (with better survival and better LV function by echo) as seen with Kawasaki disease.
4. Anticongestive measures include rapid-acting diuretics (e.g., furosemide or ethacrynic acid), rapid-acting inotropic agents (e.g., isoproterenol, dobutamine, or dopamine), administration of oxygen, and bed rest. An ACE inhibitor (e.g., captopril) may be beneficial in the acute phase. Later, digoxin may be given cautiously, using half of the usual digitalizing dose, as some patients with myocarditis are exquisitely sensitive to digoxin.
5. Arrhythmias should be treated aggressively; the use of IV amiodarone may be required.
6. The role of corticosteroids is unclear except for the treatment of severe rheumatic carditis.
7. Specific therapies: Antitoxin used in diphtheric myocarditis.

III. PERICARDITIS

Etiology

1. Viral infection is probably the most common cause, particularly in infancy.
2. Acute rheumatic fever is a common cause of pericarditis in older children in certain parts of the world.
3. Bacterial infection (purulent pericarditis). Commonly encountered are *S. aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, and streptococci.

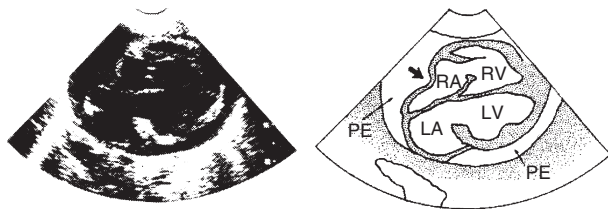
4. Tuberculosis (an occasional cause of constrictive pericarditis with insidious onset).
5. Heart surgery (postpericardiotomy syndrome).
6. Collagen disease such as rheumatoid arthritis.
7. A complication of oncologic disease or its therapy, including radiation.
8. Uremia (uremic pericarditis).

Pathology and Pathophysiology

1. Pericardial effusion may be serofibrinous, hemorrhagic, or purulent. Effusion may be completely reabsorbed or may result in pericardial thickening or chronic constriction (constrictive pericarditis).
2. Symptoms and signs of pericardial effusion are determined by two factors: speed of fluid accumulation and competence of the myocardium. A slow accumulation of a large amount of fluid may be well tolerated by stretching of the pericardium, if the myocardium is intact. A rapid accumulation of even a small amount of fluid in the presence of myocarditis can produce circulatory embarrassment.
3. With the development of pericardial tamponade, several compensatory mechanisms are called on: systemic and pulmonary venous constriction (to improve diastolic filling), an increase in the SVR (to raise falling blood pressure), and tachycardia (to improve cardiac output).

Clinical Manifestations

1. Precordial pain (dull, aching, or stabbing) with occasional radiation to the shoulder and neck may be a presenting complaint. The pain may be relieved by leaning forward and made worse by supine position or deep inspiration.
2. Pericardial friction rub is the cardinal physical sign. The heart is hypodynamic, and heart murmur is usually absent. In children with purulent pericarditis, septic fever (101° to 105° F, or 38° to 41° C), tachycardia, chest pain, and dyspnea are almost always present. Signs of cardiac tamponade may be present (distant heart sounds, tachycardia, pulsus paradoxus, hepatomegaly, neck vein distention, and occasional hypotension with peripheral vasoconstriction).
3. The ECG may show a low-voltage QRS complex, ST segment shift, and T wave inversion.
4. Chest radiographs may show a varying degree of cardiomegaly. Water bottle-shaped heart and increased pulmonary venous markings are seen with large effusion.
5. Echo is the most useful tool in establishing the diagnosis of pericardial effusion. It appears as an echo-free space between the epicardium (visceral pericardium) and the parietal pericardium.
 - a. Small pericardial effusion first appears posteriorly in the dependent portion of the pericardial sac. A small amount of fluid, which appears only in systole, is normal. With larger effusion, the fluid also appears anteriorly. With very large effusions, the swinging motion of the heart may be imaged.

**FIGURE 12-1**

Subcostal four-chamber view demonstrating pericardial effusion (PE) and collapse of the right atrial wall (*arrow*), a sign of cardiac tamponade.

- b. The following are helpful 2D echo findings of cardiac tamponade.
 - (1) Tamponade usually occurs with circumferential effusion.
 - (2) Collapse of the RA in late diastole (Fig. 12-1) is seen in subcostal views (because the pressure in the pericardial sac exceeds the pressure within the RA at end-diastole when the atrium has emptied).
 - (3) Diastolic collapse or indentation of the RV free wall, especially the outflow tract, best seen in parasternal long axis view.

Management

1. Pericardiocentesis or surgical drainage to identify the cause of the pericarditis is mandatory, especially when purulent or tuberculous pericarditis is suspected. A drainage catheter may be left in place with intermittent low-pressure drainage.
2. Pericardial fluid studies include cell counts and differential, glucose, and protein concentrations; histologic examination of cells; Gram and acid-fast stains; and viral, bacterial, and fungal cultures.
3. For cardiac tamponade, urgent decompression by surgical drainage or pericardiocentesis is indicated. While getting ready for the procedure, fluid push with Plasmanate should be given to increase central venous pressure and thereby improve cardiac filling, which can provide temporary emergency stabilization.
4. Urgent surgical drainage of the pericardium is indicated when purulent pericarditis is suspected. This must be followed by IV antibiotic therapy for 4 to 6 weeks.
5. There is no specific treatment for viral pericarditis.
6. Salicylates are given for precordial pain in patients with nonbacterial or rheumatic pericarditis.
7. Corticosteroid therapy may be indicated in children with severe rheumatic carditis or postpericardiotomy syndrome.

IV. CONSTRICTIVE PERICARDITIS

Causes and Pathology

1. Although rare in children, constrictive pericarditis may be associated with an earlier viral pericarditis, tuberculosis, incomplete drainage

of purulent pericarditis, hemopericardium, mediastinal irradiation, neoplastic infiltration, or connective tissue disorders.

2. In this condition, a fibrotic, thickened, and adherent pericardium restricts diastolic filling of the heart.

Clinical Manifestations

1. Distended jugular veins, hepatomegaly with ascites, and systemic edema may be present. Diastolic pericardial knock, which resembles the opening snap, is often heard along the left sternal border in the absence of heart murmur.
2. Chest radiographs may show calcification of the pericardium, enlargement of the superior vena cava (SVC) and left atrium (LA), and pleural effusion.
3. The ECG may show low QRS voltages, T-wave inversion or flattening, and LAH. Atrial fibrillation occasionally is seen.
4. Echo findings.
 - a. Two-dimensional echo shows (1) a thickened pericardium, (2) dilated IVC and hepatic vein, and (3) paradoxical septal motion and abrupt displacement of the interventricular septum during early diastolic filling ("septal bounce") (not specific for this condition).
 - b. M-mode echo may reveal two parallel lines representing the thickened visceral and parietal pericardia or multiple dense echoes.
 - c. Doppler examination of the mitral inflow reveals findings of diastolic dysfunction (see Fig. 11-2) and a marked respiratory variation in diastolic inflow tracings.
5. Cardiac catheterization may document the presence of constrictive physiology.
 - a. The RA and LA pressures, ventricular end-diastolic pressures, and PA wedge pressure are all elevated and usually equalized.
 - b. Ventricular pressure waveforms demonstrate the characteristic "square root sign" (in which there is an early rapid fall in diastolic pressure followed by a rapid rise to an elevated diastolic plateau).

Treatment

The treatment for constrictive pericarditis is complete resection of the pericardium; symptomatic improvement occurs in 75% of patients.

V. KAWASAKI DISEASE

Etiology and Epidemiology

1. The cause of Kawasaki disease (KD) is not known. It may be related to abnormalities of the immune system initiated by an infectious insult.
2. It peaks in winter and spring in the United States. It occurs primarily in young children; 80% of the patients are younger than age 4 years, 50% are younger than age 2 years, and cases in children older than 8 years and younger than 3 months are rarely reported.

Pathology

1. During the first 10 days after the onset of fever, a multisystem vasculitis develops, which has the greatest predilection for the coronary arteries. Other arteries such as iliac, femoral, axillary, and renal arteries are less frequently involved.
2. Coronary artery (CA) aneurysm may develop in 15% to 20% of patients.
3. There is also pancarditis, involving the AV conduction system (which can produce AV block), myocardium (myocardial dysfunction, CHF), pericardium (pericardial effusion), and endocardium (with AV valve involvement).
4. Late changes (after 40 days) consist of healing and fibrosis in the CAs, with thrombus formation and stenosis in the postaneurysmal segment and myocardial fibrosis from old myocardial infarction.
5. The elevated platelet count seen in this condition contributes to coronary thrombosis.

Clinical Manifestations

The clinical course of the disease may be divided into three phases: acute, subacute, and convalescent.

1. Acute phase (first 10 days)
 - a. Six signs that comprise the principal clinical features of KD are present during the acute phase (see [Box 12-5](#)).
 - (1) Abrupt onset of fever, usually $>39^{\circ}\text{C}$ (102°F) and often $>40^{\circ}\text{C}$ (104°F); fever persists for a mean of 11 days without treatment.
 - (2) Bilateral conjunctivitis without exudate, which resolves rapidly.
 - (3) Changes in the lips and oral cavity: erythema, dryness, fissuring, and bleeding of the lips, “strawberry tongue,” and diffuse erythema of the oropharynx.
 - (4) Changes in extremities: erythema of the palms and soles, firm edema, and sometimes painful induration.
 - (5) Diffuse maculopapular eruption involving the trunk, extremities, and perineal region; desquamation usually occurs by days 5 to 7.
 - (6) Unilateral cervical lymphadenopathy, usually $>1.5\text{ cm}$, in approximately 50% of patients.
 - b. Abnormal CV findings may include some or all of the following: tachycardia, gallop rhythm, and/or other signs of heart failure, MR murmur, cardiomegaly on chest radiographs. The ECG may show arrhythmias, prolonged PR interval (occurring in up to 60%), nonspecific ST-T change, or abnormal Q waves (wide and deep) suggestive of myocardial infarction.
 - c. Echocardiography
 - (1) Coronary artery (CA) aneurysm rarely occurs before day 10 of illness. Echo studies may show CA abnormalities at the end of the first week through the second week of illness.
 - (2) Aneurysms of the CA are classified as *saccular* (nearly equal axial and lateral diameters), *fusiform* (symmetric dilatation with

gradual proximal and distal tapering), and *ectatic* (dilated without segmental aneurysm). “Giant” aneurysm is present when the diameter of the aneurysm is ≥ 8 mm.

- (3) Normal data on the size of the proximal CAs are shown in Appendix D (Table D-6). A coronary dimension that is greater than $+3SD$ in one of the three segments (left main coronary artery [LMCA], left anterior descending [LAD], and right coronary artery [RCA]) or one that is greater than $+2.5 SD$ in two proximal segments is considered abnormal.
- (4) During the first 10 days of illness before CA aneurysm appears, other echo findings suggestive of cardiac involvement may appear: perivascular brightness and ectasia (dilatation), LV enlargement with decreased LV systolic function, mild MR, and pericardial effusion.
- d. Involvement of other organ systems is also frequent during the acute phase.
 - (1) Arthritis or arthralgia of multiple joints (30%)
 - (2) Sterile pyuria (60%)
 - (3) Abdominal pain with diarrhea (20%), liver dysfunction (40%), hydrops of the gallbladder (10%, demonstrable by abdominal ultrasound) with jaundice
 - (4) Irritability, lethargy or semicoma, and aseptic meningitis (25%)
- e. Laboratory studies. Even though laboratory results are nonspecific, they provide diagnostic support of the disease during the acute phase.
 - (1) Marked leukocytosis with a shift to the left and anemia are common.
 - (2) Acute phase reactant levels (C-reactive protein levels [CRP], erythrocyte sedimentation rate [ESR]) are always elevated, which is uncommon with viral illnesses. Normal ESR is inconsistent with the diagnosis of KD. An elevated sedimentation rate (but not CRP) can be caused by IVIG infusion per se.
 - (3) Thrombocytosis (usually $>450,000/\text{mm}^3$) occurs after day 7 of the illness, sometimes reaching 600,000 to >1 million/ mm^3 during the subacute phase. Low platelet count suggests viral illness.
 - (4) Elevated liver enzymes (>2 times the upper limit of normal) in 40% of patients, hypoalbuminemia, and mild hyperbilirubinemia may be present in 10%.
2. Subacute phase (11 to 25 days after onset)

The following clinical findings are seen during the subacute phase.

 - a. Desquamation of the tips of the fingers and toes takes place (within 2 to 3 weeks of illness).
 - b. Rash, fever, and lymphadenopathy disappear.
 - c. Significant cardiovascular changes, including coronary aneurysm (seen in approximately 20%), pericardial effusion, CHF, and myocardial infarction, can occur in this phase.
 - d. Thrombocytosis also occurs during this period (peaking at 2 weeks or more after the onset of the illness).

3. Convalescent phase

This phase lasts until the elevated ESR and platelet count return to normal. Deep transverse grooves (Beau lines) may appear across the fingernails and toenails.

Natural History

1. It is a self-limited disease for most patients.
2. However, CA aneurysm occurs in 15% to 25% of patients and is responsible for myocardial infarction (fewer than 5%) and mortality (1% to 5%). If the CA remains normal throughout the first month after onset, subsequent development of a coronary lesion is extremely unusual. However, it may be wise to repeat the echo study at 8 weeks after the onset of the illness to comfortably rule out CA involvement.
3. CA aneurysm has a tendency to regress within a year in about 50% of patients, but these arteries do not dilate normally in response to exercise or coronary vasodilators.
4. In some patients, stenosis, tortuosity, and thrombosis of the coronary arteries result.

Diagnosis

1. The diagnosis of KD is based on clinical findings. [Box 12-5](#) lists the principal clinical features that establish the diagnosis.

BOX 12-5

PRINCIPAL CLINICAL FEATURES FOR DIAGNOSIS OF KAWASAKI DISEASE

1. Fever persisting at least 5 days
2. Presence of at least 4 of the following principal features
 - a. Changes in extremities:
 - (1) Acute: Erythema of palms and soles; edema of hands and feet
 - (2) Subacute: Periungual peeling of fingers and toes in weeks 2 and 3
 - b. Polymorphous exanthema
 - c. Bilateral bulbar conjunctival injection without exudate
 - d. Changes in the lips and oral cavity: erythema, lips cracking, strawberry tongue, diffuse injection of oral and pharyngeal mucosa
 - e. Cervical lymphadenopathy (>1.5 cm in diameter), usually unilateral
3. Exclusion of other diseases with similar findings (see text)

DIAGNOSIS OF KAWASAKI DISEASE

1. Diagnosis of Kawasaki disease is made in the presence of ≥ 5 days of fever and ≥ 4 of the 5 principal clinical features listed under 2 (above)
2. Patients with fever ≥ 5 days and < 4 principal criteria can be diagnosed with Kawasaki disease when coronary artery abnormalities are detected by 2D echo or angiography
3. In the presence of ≥ 4 principal criteria plus fever, Kawasaki disease diagnosis can be made on day 4 of illness

Modified from Newburger JW, Takahashi M, Gerber MA et al: Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association, *Pediatrics* 114:1708-1733, 2004.

- a. Fever for ≥ 5 days and at least 4 of the 5 principal criteria establish the diagnosis of KD (see [Box 12-5](#)). Lymphadenopathy is present only in 50% of cases.
- b. When CA abnormality is detected, fever for ≥ 5 days and fewer than 4 criteria can be diagnosed as having KD. However, CA aneurysm rarely occurs before day 10 of the disease. During this period, perivascular brightness or ectasia (dilatation) of the CA, decreased LV systolic function, mild MR, or pericardial effusion may be present instead.
2. Incomplete (preferable to “atypical”) KD with 2 or 3 principal features creates a management problem (due to serious consequences of not giving IVIG). Therefore, patients with incomplete KD + abnormal acute phase reactants + ≥ 3 abnormal supplemental laboratory tests (shown below) may be given IVIG treatment. Even if there are < 3 abnormal lab tests, abnormal echo findings qualifies for treatment.
 - a. Acute phase reactants (with abnormal values): CRP (≥ 3.0 mg/dL) and ESR (≥ 40 mm/hr).
 - b. Other supplemental laboratory tests (with their abnormal values): (a) serum albumin (≤ 3.0 g/dL), (b) anemia for age, (c) alanine aminotransferase (> 50 or 60 U/L), (d) platelets after 7 days ($\geq 450,000/\text{mm}^3$), (e) white blood cell count ($\geq 15,000/\text{mm}^3$), and (f) urine white cell (≥ 10 cells/high power field).
3. Differential diagnoses of KD include the following.
 - a. Measles and group A β -hemolytic streptococcal infection most closely mimic KD.
 - b. Others include: viral infections (e.g., measles, adenovirus, enterovirus, Epstein-Barr virus), scarlet fever, staphylococcal scalded skin syndrome, toxic shock syndrome, bacterial cervical lymphadenopathy, drug hypersensitivity reaction, Stevens-Johnson syndrome, juvenile rheumatoid arthritis, and Rocky Mountain spotted fever.

Management

Two goals of therapy are (a) reduction of inflammation within the CA and (b) prevention of thrombosis by inhibition of platelet aggregation.

1. A high-dose (2 g/kg), single infusion of intravenous immune globulin (IVIG) with aspirin (80 to 100 mg/kg per day) given within 10 days (preferably within 7 days) of illness is considered the treatment of choice. Following IVIG infusion, two thirds of patients become afebrile by 24 hours after completion of infusion; 90% are afebrile by 48 hours.
2. A repeat dose (2 g/kg) of IVIG is indicated in children with a persistent fever.
 - a. IVIG given before 5 days of illness appears no more likely to prevent coronary aneurysm but is associated with increased need for retreatment with gamma globulin for persistent or recrudescing fever.

- b. IVIG should be given even after day 10 of illness if the patient has persistent fever, aneurysms, or ongoing systemic inflammation (by ESR or CRP).
3. Aspirin is reduced to 3 to 5 mg/kg/day in a single dose after the child has been afebrile for 48 to 72 hours. Some physicians continue the high-dose aspirin until day 14 of illness. Aspirin is continued until the patient shows no evidence of coronary changes by 6 to 8 weeks after the onset of illness. For children who develop CA abnormalities, aspirin may be continued indefinitely.
4. The usefulness of steroids in the initial treatment of KD is not well established at this time. However, steroids may be used along with IVIG for patients who continue to be febrile despite two or more courses of IVIG.
5. Recently, administration of infliximab (an antiinflammatory agent, approved for use in children with Crohn disease), has increased in the United States, despite the absence of clinical evidence of its efficacy.
6. In patients with coronary artery aneurysm, antiplatelet agents with or without an anticoagulant are indicated, depending on the severity of the involvement.
 - a. For mild and stable disease, low-dose aspirin may be appropriate.
 - b. For more severe coronary involvement, aspirin combined with other antiplatelet agents (e.g., dipyridamole [Persantine], clopidogrel [Plavix]) may be used.
 - c. For giant aneurysm or the combination of stenosis and aneurysm, low-dose aspirin together with warfarin (with INR maintained at 2.0 to 2.5) should be used.
7. Serial follow-up is important for evaluation of the cardiac status. The recommendations of the AHA are shown in [Table 12-2](#).

VI. ACUTE RHEUMATIC FEVER

Etiology

Acute rheumatic fever is a delayed sequela of group A hemolytic streptococcal infection of the pharynx (but not of the skin). The peak incidence is at 8 years (range 6 to 15 years).

Clinical Manifestations

1. The patient may have had streptococcal pharyngitis 1 to 5 weeks (average 3 weeks) before the onset of symptoms. The latent period may be as long as 2 to 6 months (average 4 months) in cases of isolated chorea.
2. Clinical manifestations of acute rheumatic fever may be grouped into (a) five major criteria, (b) four minor criteria, and (c) supporting evidence of preceding streptococcal infection ([Box 12-6](#)).
3. Major manifestations
 - a. Arthritis involving large joints (knees, ankles, elbows, wrists) is the most common manifestation (60% to 85%). Often more than one

TABLE 12-2

FOLLOW-UP RECOMMENDATIONS ACCORDING TO THE DEGREE OF CORONARY ARTERY INVOLVEMENT

RISK LEVEL	PHARMACOLOGIC THERAPY	PHYSICAL ACTIVITY	FOLLOW-UP AND DIAGNOSTIC TESTING	INVASIVE TESTING
I No coronary artery changes at any stage of illness	None beyond first 6–8 weeks (Aspirin for first 6–8 weeks only)	No restrictions beyond first 6–8 weeks	Cardiovascular risk assessment, counseling at 5-year intervals	None recommended
II Transient coronary artery ectasia disappears within first 6–8 weeks	None beyond first 6–8 weeks (Aspirin for first 6–8 weeks only)	No restrictions beyond initial 6–8 weeks	Cardiovascular risk assessment and counseling at 3- to 5-year intervals	None recommended
III One small to medium coronary artery aneurysm/major coronary artery	Low-dose aspirin (3–5 mg/kg/day), at least until aneurysm regression documented	For patients <11 years old, no restrictions beyond initial 6–8 weeks For patients 11–20 years old, physical activity guided by stress test or myocardial perfusion scan every 2 years Contact or high-impact sports discouraged for patients taking antiplatelet agents	Annual cardiology follow-up with echocardiogram and ECG Cardiovascular risk assessment and counseling Stress test with myocardial perfusion scan every 2 years in patients >10 years old	Angiography if noninvasive test suggests ischemia

Continued

TABLE 12-2

FOLLOW-UP RECOMMENDATIONS ACCORDING TO THE DEGREE OF CORONARY ARTERY INVOLVEMENT (Continued)

RISK LEVEL	PHARMACOLOGIC THERAPY	PHYSICAL ACTIVITY	FOLLOW-UP AND DIAGNOSTIC TESTING	INVASIVE TESTING
IV One or more large or giant coronary artery aneurysms, or multiple or complex aneurysms in same coronary artery without obstruction	Long-term aspirin (3-5 mg/kg/day) and warfarin (target: INR 2.0-2.5) or low-molecular heparin (target: antifactor Xa level 0.5-1.0 U/ml) should be combined in giant aneurysm	Contact or high-impact sports should be avoided because of risk of bleeding Other physical activity recommendations guided by annual stress test or myocardial perfusion evaluation	Cardiology follow-up with echocardiogram and ECG every 6 months Annual stress test with myocardial perfusion evaluation For females of child-bearing age, reproductive counseling is recommended	First angiography at 6-12 months or sooner if clinically indicated Repeat angiography if noninvasive test, clinical, or laboratory findings suggest ischemia Elective repeat angiography under some circumstances (atypical anginal pain, inability to do stress testing, etc.)
V Coronary artery obstruction	Long-term low-dose aspirin (3-5 mg/kg/day) Warfarin or low-molecular weight heparin if giant aneurysm persists Consider use of β -blocker to reduce myocardial oxygen consumption	Contact or high-impact sports should be avoided because of risk of bleeding Other physical activity recommendations guided by stress test or myocardial perfusion scan	Cardiology follow-up with echocardiogram and ECG every 6 months Annual stress test or myocardial perfusion scan For females of child-bearing age, reproductive counseling is recommended	Angiography recommended to address therapeutic options of bypass grafting or catheter intervention

Modified from Newburger JW, Takahashi M, Gerber MA et al: Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. *Pediatrics* 114:1708-1733, 2004.

BOX 12-6

GUIDELINES FOR THE DIAGNOSIS OF INITIAL ATTACK OF RHEUMATIC FEVER (JONES CRITERIA, 1992)

Major Manifestations	Minor Manifestations
Carditis	Clinical Findings
Polyarthrititis	Arthralgia
Chorea	Fever
Erythema marginatum	
Subcutaneous nodule	Laboratory Findings
	Elevated acute-phase reactants (ESR, C-reactive protein)
	Prolonged PR interval

PLUS

Supporting Evidence of Antecedent Group A Streptococcal Infection

Positive throat culture or rapid streptococcal antigen test

Elevated or rising streptococcal antibody titer

Diagnosis of **RHEUMATIC FEVER** is *highly probable*, if there are:

1. Two major manifestations or 1 major and 2 minor manifestations, *and*
2. Evidence of preceding group A streptococcal infection.

ESR, erythrocyte sedimentation rate.

From Special Writing Group of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council of Cardiovascular Disease in the Young, American Heart Association. *Circulation* 87:302-307, 1993.

- joint, either simultaneously or in succession, is involved, with the characteristic migratory nature of the arthritis. Swelling, heat, redness, severe pain, tenderness, and limitation of motion are common. The arthritis responds dramatically to antiinflammatory salicylate therapy; if patients treated with salicylates do not improve within 48 hours, the diagnosis of acute rheumatic fever probably is incorrect. Arthritis subsides in a few days to weeks even without treatment and does not cause permanent damage.
- b. Carditis affects 40% to 50% of patients. Mild carditis disappears rapidly in weeks, but severe carditis may last for months. Only carditis can cause permanent cardiac damage. Signs of carditis include some or all of the following:
- (1) Tachycardia (out of proportion for the degree of fever).
 - (2) A heart murmur of MR and/or AR is frequently present. Although the Jones criteria require the presence of audible MR and/or AR murmur to make the diagnosis of acute rheumatic carditis, inclusion of echo abnormalities may enhance correct diagnosis of acute rheumatic fever (see below).
 - (3) Pericarditis (friction rub, pericardial effusion, chest pain, and ECG changes).
 - (4) Cardiomegaly on chest radiograph (caused by pericarditis, pancarditis, or CHF).
 - (5) Signs of CHF (gallop rhythm, distant heart sounds, and cardiomegaly).

- (6) The following are echo abnormalities seen in acute rheumatic fever.
- (a) Gross prolapse of the mitral valve or the presence of postero-lateral (but not central) MR jet by color flow mapping may be significant. With chronic rheumatic MR, the regurgitation jets tend to be more central.
 - (b) Other abnormal echo findings may include pericardial effusion, increased LV dimension, or impaired LV function.
- c. Erythema marginatum (10%), with the characteristic nonpruritic serpiginous or annular erythematous rashes, is most prominent on the trunk and the inner proximal portions of the extremities. The rashes are evanescent, disappearing on exposure to cold and reappearing after a hot shower or when the patient is covered with a warm blanket.
- d. Subcutaneous nodules (2% to 10%) are hard, painless, nonpruritic, freely movable swellings, 0.2 to 2 cm in diameter. They are usually found symmetrically, singly or in clusters, on the extensor surfaces of both large and small joints, over the scalp, or along the spine. They are not transient, lasting for weeks, and have a significant association with carditis. They are also found in conditions other than rheumatic fever (such as rheumatoid arthritis and systemic lupus erythematosus).
- e. Sydenham chorea, or St. Vitus dance (15%), is found more often in prepubertal (8 to 12 years) girls than in boys. It is a neuropsychiatric disorder consisting of both neurologic disorders (choreic movement and hypotonia) and psychiatric components (such as emotional lability, hyperactivity, separation anxiety, obsessions, and compulsions). It begins initially with emotional lability and personality changes, soon (in 1 to 4 weeks) replaced by the characteristic spontaneous, purposeless movement of chorea, which is followed by motor weakness. The choreic movements last for an average of 7 months (and up to 17 months) before slowly waning in severity. It is often an isolated manifestation; the patient may have no fever, and erythrocyte sedimentation rate (ESR) and antistreptolysin O (ASO) titers may be normal. Recently, elevated titers of “antineuronal antibodies” recognizing basal ganglion tissues have been found in over 90% of patients, suggesting that chorea may be related to dysfunction of basal ganglia and cortical neuronal components.
4. Minor manifestations include fever, arthralgia, elevated acute-phase reactants (elevated ESR and CRP), and prolonged PR interval (see [Box 12-6](#)).
5. Evidence of antecedent group A streptococcal infection.
- a. Specific antibody tests are the most reliable laboratory evidence of antecedent streptococcal infection capable of producing acute rheumatic fever. An ASO titer above 333 Todd units in children or above 250 Todd units in adults is considered significant. Antideoxyribonuclease B titer of 240 Todd units or more in children or 120 Todd units or more in adults is considered elevated.
 - b. History of sore throat or scarlet fever, positive throat culture, and rapid streptococcal antigen tests (Streptozyme test) for group A streptococci are less reliable than the antibody test.

Diagnosis

1. Diagnosis of acute rheumatic fever is highly probable in the presence of either two major manifestations or one major plus two minor mani-
festations PLUS evidence of antecedent streptococcal infection. The
absence of supporting evidence of a preceding Group A streptococcal
infection makes the diagnosis doubtful (see Box 12-6).
2. Arthralgia or a prolonged PR interval cannot be used as a minor mani-
festation in the presence of arthritis and carditis, respectively.
3. The following are exceptions to the Jones criteria: (1) Chorea may
occur as the only manifestation of rheumatic fever, (2) indolent cardi-
tis may be the only manifestation in a patient who comes to medical
attention months after the onset of rheumatic fever, and (3) occasion-
ally, patients with rheumatic fever recurrences may not fulfill the Jones
criteria.

Management

1. When acute rheumatic fever is suspected, the following laboratory
studies are obtained: CBC, acute phase reactants (ESR, C-reactive
protein), throat culture, ASO titer, chest radiograph, and ECG.
Cardiology consultation is recommended early to clarify any cardiac
involvement; 2D echo and Doppler studies are usually performed at
that time.
2. Benzathine penicillin G, 0.6 million to 1.2 million units, is admin-
istered IM to eradicate *Streptococcus* (and as the first injection for
prevention of recurrence). In patients allergic to penicillin, erythro-
mycin, 40 mg/kg/day in two to four doses for 10 days, may be substi-
tuted for penicillin.
3. Bed rest of different levels is recommended (Table 12-3), which is
followed by a period of indoor ambulation before the child is allowed to
go back to school. Full activity is allowed later, when the ESR returns to
normal, except for children with significant cardiac involvement.
4. Therapy with antiinflammatory agents should be started as soon as the
diagnosis of acute rheumatic fever has been established.
 - a. For arthritis, aspirin therapy is continued for 2 weeks and gradually
withdrawn over the following 2 to 3 weeks. Rapid resolution of joint
symptoms with aspirin within 24 to 36 hours is supportive evidence
of acute rheumatic fever.

TABLE 12-3
GENERAL GUIDE FOR BED REST AND AMBULATION

	ARTHRITIS ALONE	MILD CARDITIS	MODERATE CARDITIS	SEVERE CARDITIS
Bed rest	1-2 wk	3-4 wk	4-6 wk	As long as CHF is present
Ambulation	1-2 wk	3-4 wk	4-6 wk	2-3 mo

Mild carditis, questionable cardiomegaly; Moderate carditis, definite but mild cardiomegaly; Severe carditis, marked cardiomegaly or heart failure.

- b. For mild to moderate carditis, aspirin alone is recommended in a dose of 90 to 100 mg/kg/day in four to six divided doses (target blood level of salicylate 20 to 25 mg/100 mL).
- c. For severe carditis, prednisone, 2 mg/kg/day in four divided doses may be added to aspirin therapy for 2 to 6 weeks.
- 5. Management of Sydenham chorea.
 - a. Reduce physical and emotional stress and use protective measures as indicated.
 - b. Give benzathine penicillin G, 1.2 million units, just as in patients with other rheumatic manifestations.
 - c. Antiinflammatory agents are not needed in patients with isolated chorea.
 - d. For severe cases, any of the following drugs may be used: Pheno-barbital, haloperidol, valproic acid, chlorpromazine (Thorazine), diazepam (Valium), or steroids.
 - e. Results of plasma exchange (to remove antineuronal antibodies) and IV immune globulin therapy (to inactivate the effects of the antineu-ronal antibodies) are promising in decreasing the severity of chorea.

Prevention

- 1. Any patient with a documented history of rheumatic fever, including those with isolated chorea and those without evidence of rheumatic heart disease, must receive prophylaxis.
- 2. Benzathine penicillin G, 600,000 units for patients under 60 lbs (27 kg) and 1.2 million units for patients over 60 lbs, given IM every 28 days (not once a month), is the method of choice.
- 3. Although less effective, the following alternative drugs may be used:
 - a. Oral penicillin V, 250 mg twice daily.
 - b. Oral sulfadiazine, 1 g or sulfisoxazole 0.5 g once daily.
 - c. If the patient is allergic to penicillin, erythromycin, 250 mg twice daily, may be used.
- 4. Recommended duration of prophylaxis for rheumatic fever is summa-rized in [Table 12-4](#).

TABLE 12-4
RECOMMENDED DURATION OF PROPHYLAXIS FOR RHEUMATIC FEVER

CATEGORY	DURATION
Rheumatic fever without carditis	At least for 5 years or until 21 years of age, whichever is longer
Rheumatic fever with carditis but without residual heart disease (no valvular disease)	At least for 10 years or well into adulthood, whichever is longer
Rheumatic fever with carditis and residual heart disease (persistent valvular disease)	At least 10 years since last episode and at least until age 40 years; sometimes lifelong prophylaxis

From Dajani A, Taubert K, Ferrieri P et al: Treatment of acute streptococcal pharyngitis and prevention of rheumatic fever: a statement for health professionals, *Pediatrics* 96:758-764, 1995.

Valvular Heart Disease

Valvular heart disease is either congenital or acquired. Many congenital valvular abnormalities are associated with other major defects. A relatively isolated form of valvular heart disease is rheumatic in origin, which still occurs in some parts of the world. Among rheumatic heart disease, mitral valve involvement occurs in about three fourths and aortic valve involvement in about one fourth of the cases. Rheumatic involvement of the tricuspid and pulmonary valves almost never occurs. Although the cause of mitral valve prolapse (MVP) is not entirely clear, it is discussed in this chapter.

I. MITRAL STENOSIS

Prevalence

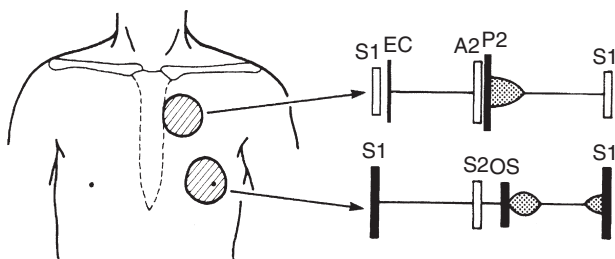
MS of rheumatic origin is rare in children (because it requires 5 to 10 years from the initial attack to develop the condition), but it is the most common valvular involvement in adult rheumatic patients in areas where rheumatic fever is still prevalent.

Pathology and Pathophysiology

1. In rheumatic MS, thickening of the leaflets and fusion of the commissures dominate the pathologic findings. Calcification with immobility of the valve results over time.
2. A significant MS results in the enlargement of the LA, pulmonary venous hypertension, and pulmonary artery hypertension with resulting enlargement and hypertrophy of the right side of the heart.
3. In patients with severe MS, pulmonary congestion and edema, fibrosis of the alveolar walls, hypertrophy of the pulmonary arterioles, and loss of lung compliance result.

Clinical Manifestations

1. Children with mild MS are asymptomatic. With significant MS, dyspnea with or without exertion is the most common symptom in older children. Orthopnea, nocturnal dyspnea, or palpitation is present in more severe cases.
2. Neck veins are distended if right-sided heart failure supervenes. A loud S1 at the apex and a narrowly split S2 with accentuated P2 are audible if pulmonary hypertension is present (Fig. 13-1). An opening snap (a short snapping sound accompanying the opening of the mitral valve) and a low-frequency mitral diastolic rumble may be present at the apex. A crescendo presystolic murmur may be audible at the apex. Occasionally, a high-frequency diastolic murmur of PR (Graham Steell murmur) is present at the ULSB in patients with pulmonary hypertension.

**FIGURE 13-1**

Cardiac findings of MS. Abnormal sounds are shown in black and include a loud S1, an ejection click (EC), a loud S2, and an opening snap (OS). Also note the mid-diastolic rumble and presystolic murmur. The murmur of pulmonary insufficiency indicates long-standing pulmonary hypertension.

3. The ECG may show RAD, LAH, and RVH (caused by pulmonary hypertension). Atrial fibrillation is rare in children.
4. Chest radiographs show enlargement of the LA and RV. The main PA segment is usually prominent. Lung fields show pulmonary venous congestion, interstitial edema shown as Kerley B lines (dense, short, horizontal lines most commonly seen in the costophrenic angles), and redistribution of pulmonary blood flow with increased pulmonary vascularity to the upper lobes.
5. Echo studies provide accurate diagnosis of MS.
 - a. Dilated LA, RV, and RA and prominent main PA are imaged.
 - b. A mean Doppler gradient of <4-5 mm Hg results from mild stenosis, 6-12 mm Hg from moderate stenosis, and >13 mm Hg from severe stenosis.
 - c. RV systolic pressure can be estimated from the TR jet velocity.

Natural History

1. Most children with mild MS are asymptomatic but become symptomatic with exertion.
2. Atrial flutter or fibrillation and thromboembolism (related to the chronic atrial arrhythmias) are rare in children.
3. Hemoptysis can develop from the rupture of small vessels in the bronchi as a result of long-standing pulmonary venous hypertension.

Management

Medical

1. Mild to moderate MS is managed with diuretics.
2. Balloon dilatation is an effective and safe option for children with rheumatic mitral stenosis.
3. If atrial fibrillation develops, propranolol, verapamil, or digoxin may be used to slow the ventricular rate. Intravenous procainamide may be used for conversion to sinus rhythm in hemodynamically stable patients.

4. For patients with chronic atrial fibrillation, anticoagulation with warfarin should be started 3 weeks before cardioversion to prevent systemic embolization of atrial thrombus. Anticoagulation is continued for 4 weeks after restoration of sinus rhythm. Quinidine may prevent recurrence.
- 5 Varying degrees of restriction of activity may be indicated.
6. Recurrence of rheumatic fever should be prevented with penicillin or sulfonamide (see Acute Rheumatic Fever).

Surgical

1. Indications. The ACC/AHA 2006 Guidelines for surgical indications are as follows:
 - a. Surgery is indicated in symptomatic patients (NYHA functional class III or IV) and mean Doppler MV gradient >10 mm Hg. Symptoms may include angina, syncope, or dyspnea on exertion.
 - b. Surgery is reasonable in mildly symptomatic patients (NYHA functional class I) and mean Doppler MV gradient >10 mm Hg.
 - c. Surgery is reasonable in asymptomatic patients with pulmonary artery pressure ≥ 50 mm Hg and mean MV gradient ≥ 10 mm Hg.
2. Procedures and mortality
 - a. For rheumatic MS, if balloon dilatation is unsuccessful, closed or open mitral commissurotomy remains the procedure of choice for those with pliable mitral valves without calcification or MR. The operative mortality rate is $<1\%$.
 - b. Mitral valve replacement. A prosthetic valve (Starr-Edwards, Bjork-Shiley, St. Jude) is inserted either in the annulus or in a supraannular position. The surgical mortality is 0 to 19%. All mechanical valves require anticoagulation with warfarin. Bioprostheses (porcine valve, heterograft valve) do not require anticoagulation therapy but require low-dose aspirin. Bioprostheses tend to deteriorate more rapidly due to calcific degeneration in children.

Follow-Up

1. Regular checkups every 6 to 12 months with echo and Doppler studies should be done for possible progression of the disease or dysfunction of the repaired or replaced valve.
2. After replacement with a mechanical valve with no risk factors, warfarin is indicated to achieve an INR of 2.5 to 3.5. Low-dose aspirin is also indicated.
3. After replacement with a bioprosthesis with risk factors (which may include atrial fibrillation, previous thromboembolism, LV dysfunction, and hypercoagulable state), warfarin is also indicated. When there are no risk factors after bioprosthesis placement, antiplatelet dose of aspirin alone is indicated.

II. MITRAL REGURGITATION

Prevalence

MR of rheumatic origin is rare but it is the most common valvular involvement in children with rheumatic heart disease.

Pathology

1. In rheumatic heart disease, mitral valve leaflets are shortened because of fibrosis, resulting in MR.
2. With increasing severity of MR, dilatation of the LA and LV results and the mitral valve ring may become dilated. Pulmonary hypertension may eventually develop but is less common than with MS.

Clinical Manifestations

1. Patients are usually asymptomatic with mild MR. A history of fatigue and palpitation may be present.
2. The S2 may split widely as a result of shortening of the LV ejection and early closure of the aortic valve. A loud S3 is common. The hallmark of MR is a grade 2 to 4/6 regurgitant systolic murmur at the apex, with good transmission to the left axilla (best demonstrated in the left decubitus position). A short, low-frequency diastolic rumble may be present at the apex (see Fig. 13-2).
3. The ECG is normal in mild cases. With moderate to severe MR, LVH (or LV dominance) with or without LAH may be present. Atrial fibrillation is rare in children but frequent in adults.
4. Chest radiographs may show LA and LV enlargement. Pulmonary venous congestion may develop if CHF supervenes.
5. Two-dimensional echo shows dilated LA and LV; the degree of the dilatation is related to the severity of MR. Color flow mapping of the regurgitant jet into the LA and Doppler studies can assess the severity of the regurgitation. The MR is central with rheumatic MR (and eccentric with congenital cleft mitral valve).
6. Patients are relatively stable for a long time with MR. LV failure and consequent pulmonary hypertension may develop in adult life.

Management

Medical

1. Prophylaxis against recurrence of rheumatic fever is important.
2. Activity need not be restricted in mild cases.

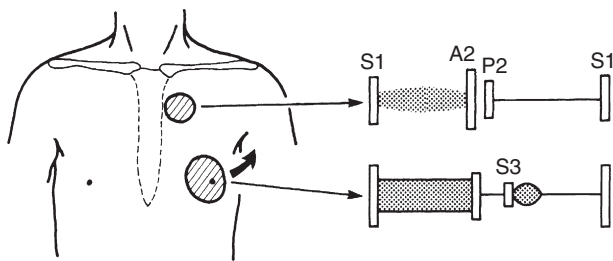


FIGURE 13-2

Cardiac findings of MR. Arrow near the apex indicates the direction of radiation of the murmur toward the axilla.

3. Afterload-reducing agents (such as ACE inhibitors) are particularly beneficial.
4. Anticongestive therapy is provided if CHF develops.
5. If atrial fibrillation develops (rare in children), propranolol, verapamil, or digoxin is indicated to slow the ventricular rate.

Surgical

1. Indications for valve surgery in adolescents and young adults with severe MR are as follows, according to the ACC/AHA 2006 Guidelines:
 - a. Symptomatic patients with severe MR with NYHA functional class III or IV
 - b. Asymptomatic patients with severe MR and LV systolic dysfunction ($EF \leq 0.6$)
 - c. Surgery may be considered in patients with preserved LV function if the likelihood of successful repair without residual MR is great.
 - d. Some centers consider an LV diastolic dimension of 60 mm in adults an indication for mitral valve replacement.
 - e. For children, intractable CHF, progressive cardiomegaly with symptoms, and pulmonary hypertension may be indications for the valve surgery.
2. Procedures and mortality:
 - a. Valve repair surgery is preferred over valve replacement in pediatric patients. For central regurgitation with dilated annulus, annuloplasty is performed by commissuroplasty. Valve repair has a lower mortality rate ($<1\%$) and anticoagulation is not necessary.
 - b. Valve replacement is rarely necessary for unrepairable regurgitation. Frequently used low-profile prostheses are the Bjork-Shiley tilting disk and the St. Jude pyrolitic carbon valve. The surgical mortality rate is 2% to 7% for valve replacement. If a prosthetic valve is used, anticoagulation therapy must be continued.

Follow-Up

1. Valve function (of either the repaired natural valve or the replacement valve) should be checked by echo and Doppler studies every 6 to 12 months before and after intervention.
2. After replacement with a mechanical valve, warfarin (to achieve an INR of 2.5 to 3.5) and low-dose aspirin are indicated.
3. After replacement with a bioprosthesis, aspirin alone is indicated at the dose of 80 mg per day, if there are no risk factors. When there are risk factors (such as atrial fibrillation, previous thromboembolism, LV dysfunction, and hypercoagulable state) warfarin is also indicated.

III. AORTIC REGURGITATION

Pathology

Sclerosis of the aortic valve results in distortion and retraction of the cusps with regurgitation of the valve. AR of rheumatic origin is almost always associated with mitral valve involvement.

Clinical Manifestations

1. Patients with mild regurgitation are asymptomatic. Exercise tolerance is reduced with more severe AR.
2. With moderate or severe AR, hyperdynamic precordium is present. A wide pulse pressure and a bounding water-hammer pulse may be present with severe AR. The S2 may be normal or single. A high-pitched diastolic decrescendo murmur, best audible at the third or fourth left intercostal space, is the auscultatory hallmark (see Fig. 13-3). This murmur is more easily audible with the patient sitting and leaning forward. The longer the murmur, the more severe is the regurgitation. A mid-diastolic mitral rumble (Austin Flint murmur) may be present at the apex when the AR is severe.
3. The ECG is normal in mild cases. In severe cases, LVH usually is present with or without LAH.
4. Chest radiographs show cardiomegaly of varying degrees involving the LV.
5. Echo studies demonstrate an increased LV dimension. The LV diastolic dimension is proportional to the severity of AR. Color flow and Doppler examination can estimate the severity of AR. LV systolic dysfunction develops at a later stage in severe AR.
6. Patients with mild to moderate AR remain asymptomatic for a long time, but once symptoms begin to develop, many patients deteriorate rapidly. Anginal pain, CHF, and multiple PVCs are unfavorable signs occurring with severe AR.

Management

Medical

1. Varying degrees of activity restriction may be indicated. Aerobic exercise is a better form of exercise; weight lifting exercises, push-ups, pull-ups, sit-ups, or similar activities are discouraged because these activities increase AR.

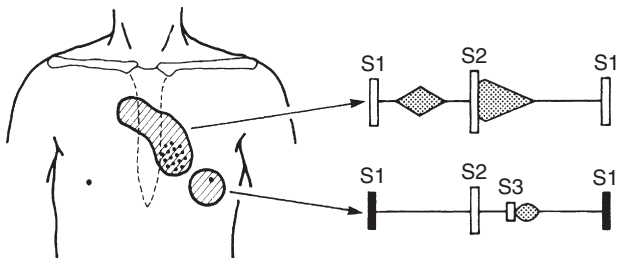


FIGURE 13-3

Cardiac findings of AR. The S1 is abnormally soft (*black bar*). The predominant murmur is a high-pitched, diastolic decrescendo murmur at the third left intercostal space.

2. ACE inhibitors have been shown to reduce the dilatation and hypertrophy of the LV in children with AR.
3. If CHF develops, digoxin, diuretics, and ACE inhibitors may be temporarily beneficial.
4. Antibiotic prophylaxis (with penicillin or sulfonamide) to prevent the recurrence of rheumatic fever is indicated.

Surgical

1. Indications. According to the ACC/AHA 2006 Guidelines, the following are surgical indications in adolescent and adult patients with chronic severe AR.
 - a. Symptomatic patients (with angina, syncope, or dyspnea on exertion).
 - b. Asymptomatic patients with LV systolic dysfunction ($EF < 0.5$) on serial studies 1 to 3 months apart.
 - c. Asymptomatic patients with progressive LV enlargement (end-diastolic dimension greater than mean $+4SD$).
2. Procedure and mortality. Aortic valve repair is favored over valve replacement whenever possible. The mortality rate for valve repair is near zero and that for valve replacement is about 2% to 5%.
 - a. Valve repair may include repair of simple tears or valvuloplasty for prolapsed cusps.
 - b. Valve replacement surgery: The antibiotic-sterilized aortic homograft appears to be the device of choice. The porcine heterograft has the risk of accelerated degeneration. The Bjork-Shiley and St. Jude prostheses require anticoagulation therapy and are less suitable for young patients.
 - c. A pulmonary root autograft (Ross procedure) may be an attractive alternative to the conventional valve replacement surgery (see Fig. 8-6). The surgical mortality rate is near zero. This procedure does not require anticoagulant therapy, the autograft may last longer than a porcine bioprosthesis, and there is a growth potential for the autograft pulmonary valve.

Follow-Up

1. Regular follow-up is required every 6 to 12 months with echo and Doppler studies before and after intervention.
2. Anticoagulation is needed after a prosthetic mechanical valve replacement. INR should be maintained between 2.5 and 3.5 for the first 3 months and 2.0 to 3.0 beyond that time. Low-dose aspirin (81 mg per day for adolescents) is also indicated in addition to warfarin.
3. After aortic valve replacement with bioprosthesis and no risk factors, low-dose aspirin (81 mg) is indicated, but warfarin is not indicated. When there are risk factors (such as atrial fibrillation, previous thromboembolism, LV dysfunction, and hypercoagulable state), warfarin is indicated to achieve an INR of 2.0 to 3.0.
4. Following Ross procedure, anticoagulation is not indicated.

IV. MITRAL VALVE PROLAPSE

Prevalence and Pathology

1. The reported incidence of MVP of 2% to 5% in the pediatric population probably is an overestimate. The prevalence of MVP increases with age. This condition is more common in adults than in children and in females than in males.
2. MVP is primary in most cases and is due to an inherited (autosomal dominant) abnormality of the mitral valve leaflets and their supporting chordae tendineae.
3. Thick and redundant mitral valve leaflets bulge into the mitral annulus (caused by myxomatous degeneration of the valve leaflets and/or the chordae).
4. MVP is often associated with heritable disorders of connective tissue disease, such as Marfan syndrome, Ehlers-Danlos syndrome, and Stickler syndrome. Nearly all patients with Marfan syndrome have MVP, progressive with advancing age.
5. MVP is sometimes seen in patients with secundum ASD.

Clinical Manifestations

1. MVP usually is asymptomatic, but a history of nonexertional chest pain, palpitation, and, rarely, syncope may be elicited. There may be a family history of MVP.
2. An asthenic build with a high incidence of thoracic skeletal anomalies (80%), including pectus excavatum (50%), straight back (20%), and scoliosis (10%), is common.
3. The midsystolic click with or without a late systolic murmur audible at the apex is the hallmark of the condition (see [Fig. 13-4](#)). The presence or absence of the click and murmur, as well as their timing, varies from one examination to the next.
 - a. The click and murmur may be brought out by held expiration, left decubitus position, sitting, standing, or leaning forward.
 - b. Various maneuvers can alter the timing of the click and the murmur:
 - (1) The click moves toward the S1 and the murmur lengthens with maneuvers that decrease the LV volume, such as standing, sitting, Valsalva strain phase, tachycardia, and the administration of amyl nitrite.
 - (2) The click moves toward the S2 and the murmur shortens with maneuvers that increase the LV volume, such as squatting, hand grip exercise, Valsalva release phase, bradycardia, and the administration of pressor agents or propranolol.
4. The ECG is usually normal but may show flat or inverted T waves in II, III, and aVF (in 20% to 60%) and, rarely, SVT, PACs, PVCs, first-degree AV block, or RBBB.
5. Chest radiographs are unremarkable except for LA enlargement seen in patients with severe MR. Thoracic skeletal abnormalities (e.g., straight back, pectus excavatum, and scoliosis) may be present.

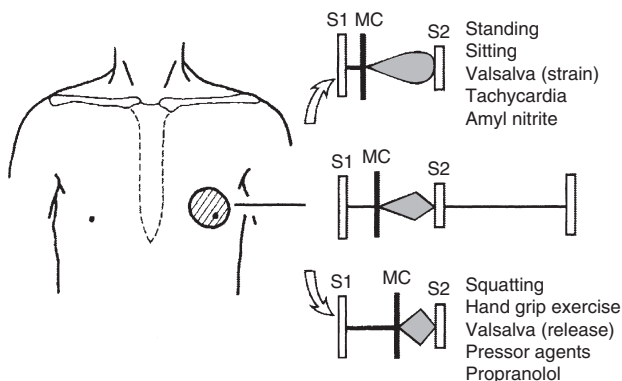
**FIGURE 13-4**

Diagram of auscultatory findings in MVP and the effect of various maneuvers on the timing of the midsystolic click (MC) and the murmur. The maneuvers that reduce ventricular volume enhance leaflet redundancy and move the click and murmur earlier in systole. An increase in LV dimension has the opposite effect.

6. Two-dimensional echo shows the following.
 - a. In adult patients, prolapse of the mitral valve leaflet(s) superior to the plane of the mitral valve seen in the parasternal long-axis view is diagnostic. The superior displacement seen only on the apical four-chamber view is not diagnostic because it occurs in more than 30% of normal individuals due to the “saddle-shaped” mitral valve ring.
 - b. In adults with MVP, one or both mitral valve leaflets bulge by at least 2 mm into the LA during systole in the parasternal long-axis view. Thickening of the involved leaflet to more than 5 mm supports the diagnosis.
 - c. Some pediatric patients with characteristic body build and auscultatory findings of the condition do not show the adult echo criterion of MVP; they may only show thickened mitral leaflets with systolic straightening or systolic superior doming and some posterosuperior displacement of the coaptation point of the mitral valve, some with mild MR. It may be because MVP is a progressive disease with the full manifestations occurring in the adult life.

Natural History

1. The majority of patients are asymptomatic, particularly during childhood.
2. Rare complications reported in adult patients, although rare in childhood, include infective endocarditis, spontaneous rupture of chordae tendineae, progressive MR, CHF, arrhythmias, conduction disturbances, and sudden death (probably from ventricular arrhythmias).

Management

1. Asymptomatic patients require no treatment or restriction of activity.
2. β -adrenergic blockers (such as propranolol or atenolol) are the drugs of choice in the following situations. Calcium channel blockers may prove to be effective in some patients.
 - a. Patients who are symptomatic (with palpitation, lightheadedness, dizziness, or syncope) secondary to ventricular arrhythmias. Symptomatic patients suspected to have arrhythmias should undergo ambulatory ECG monitoring and/or treadmill exercise testing.
 - b. Patients with self-terminating episodes of SVT.
 - c. Patients with chest discomfort may also be treated with propranolol. It is not relieved by nitroglycerine, but may worsen.
3. Antibiotic prophylaxis against infective endocarditis is recommended when significant MR is present.
4. Physical activities such as weight lifting, push-ups, pull-ups, or hanging on a monkey bar should be avoided.
5. Reconstructive surgery or mitral valve replacement rarely may be indicated in patients with severe MR.

Chapter 14

Cardiac Tumors

Prevalence

1. Cardiac tumors in the pediatric age group are very rare. A large portion of pediatric primary heart tumors (about 70%) are seen in patients less than 1 year of age.
2. Relative frequency of cardiac tumors in the pediatric age group is shown in [Table 14-1](#).
 - a. In infants younger than 1 year old, more than 50% are rhabdomyomas, followed by fibromas (25%).
 - b. In children 1 to 16 years of age, nearly 40% are fibromas and myxomas.
3. More than 90% of primary tumors are benign in infants.

Pathology

Description of three common cardiac tumors follows.

A. Rhabdomyoma

1. The most common location of rhabdomyoma is in the ventricular septum or free wall.
2. The size ranges from several millimeters to several centimeters.
3. More than 50% of the cases have tuberous sclerosis (e.g., with adenoma of the sebaceous glands, mental retardation, seizures).
4. Tumors regress in size or number or both in most patients younger than 4 years of age. Spontaneous complete regression may occur.
5. They may produce symptoms of obstruction to blood flow, ventricular arrhythmias, SVT associated with WPW preexcitation, or sudden death.

B. Fibroma

1. It usually occurs as a single solid tumor, most commonly in the ventricular septum and less commonly in the wall of any cardiac chamber.
2. The size of the tumor varies from several millimeters to centimeters.
3. The tumor may obstruct blood flow, disturb atrioventricular or intraventricular conduction, or cause arrhythmias.

C. Myxoma

1. It is the most common cardiac tumor in adults (30% of all primary cardiac tumors), but rare in infants and children.
2. The majority arise in the LA, 25% arise in the RA, and they very rarely arise in the ventricles.

TABLE 14-1
RELATIVE INCIDENCE OF CARDIAC TUMORS IN INFANTS AND CHILDREN*

TUMORS	INCIDENCE (%)	TUMORS	INCIDENCE (%)
Infant (less than 12 months) (N = 52)		Children (1-16 years of age) (N = 25)	
BENIGN TUMORS (94%)		BENIGN TUMORS (58%)	
Rhabdomyoma	52	Rhabdomyoma	8
Fibroma	25	Fibroma	21
Hemangioma/angioma	6	Myxoma	17
Teratoma	2	Hemangioma/angioma	4
Others	8	Teratoma	0
		Others	8
MALIGNANT TUMORS (6%)		MALIGNANT TUMORS (43%)	
Rhabdomyosarcoma	2	Rhabdomyosarcoma	8
Leiomyosarcoma	4	Leiomyosarcoma	2
Others	0	Others	33

*Adapted from Becker AE: Primary heart tumors in the pediatric age group: a review of salient pathologic features relevant for clinicians. *Pediatr Cardiol* 21:317-323, 2000.

3. Pedunculated myxomas commonly interfere with mitral valve function (due to intermittent protrusion through the valve) or produce thrombo-embolic phenomenon.

Clinical Manifestations

- Cardiac tumors usually are found on routine echo studies when the diagnosis is not suspected.
- Syncope or chest pain may be a presenting complaint in older children. Sudden unexpected death may be the first manifestation. Rarely, symptoms vary with posture in cases of pedunculated tumors (such as myxoma).
- Cardiac findings are nonspecific and vary primarily with the location and the size of the tumor.
 - Tumors near cardiac valves may produce heart murmurs of stenosis or regurgitation of valves.
 - Tumors involving the conduction tissue (such as seen with fibromas) may cause arrhythmias or conduction disturbances.
 - Intracavitary tumors (such as rhabdomyoma) may produce inflow or outflow obstruction.
 - Mural tumors may result in heart failure or cardiac arrhythmias.
 - Pericardial tumors, which may signal malignancy, can produce peri-cardial effusion and cardiac tamponade.
 - Fragmentation of intracavitary tumors may lead to embolism of the pulmonary or systemic circulations (as seen with myxoma).
- The ECG may show nonspecific ST-T changes, an infarct-like pattern, low-voltage QRS complexes, or WPW preexcitation. Various arrhythmias and conduction disturbances have been reported.

5. Chest radiographs may reveal altered contour of the heart with or without changes in pulmonary vascular markings.

Diagnostic Procedures

1. Two-dimensional echo is the primary diagnostic tool. Transesophageal echocardiography (TEE) can provide more precise delineation of the tumor.
 - a. Multiple intraventricular tumors are most likely rhabdomyomas.
 - b. A solitary tumor of varying size, arising from the ventricular septum or the ventricular wall, is likely to be a fibroma.
 - c. Left atrial tumors, especially when pedunculated, usually are myxomas.
 - d. An intrapericardial tumor arising near the great arteries most likely is a teratoma.
 - e. Pericardial effusion suggests a secondary malignant tumor.
2. MRI techniques have certain advantages over the echo study.
3. Cardiac catheterization and angiography are usually not necessary. Attempts at tissue diagnosis can be risky due to possible embolization of tumor fragment.

Management

1. Rhabdomyomas: Because of known tendency for spontaneous regression, surgical intervention is not indicated unless the tumors produce obstruction or arrhythmias refractory to medical treatment.
2. Fibromas: A successful complete resection of a fibroma sometimes is possible, but not always.
3. Myxomas: Surgical removal is a standard procedure and has a favorable outcome.
4. If myocardial involvement is extensive, surgical treatment is not possible. Cardiac transplantation may be an option in such cases.

Chapter 15

Cardiovascular Involvement in Systemic Diseases

Many systemic diseases may have important cardiovascular (CV) manifestations. The CV manifestations usually are evident when the diagnosis of the primary disease is made, but occasionally CV manifestations may precede evidence of the basic disease. In this chapter, CV manifestations of selected systemic diseases are presented.

DIGEORGE SYNDROME

Description

DiGeorge syndrome occurs in both males and females. Approximately 90% of patients have a deletion of the long arm of chromosome 22 (22q11.2) detectable with the fluorescence in situ hybridization (FISH) technique. Currently the term “22q11 deletion syndrome” is used.

Clinical Manifestations

Clinical features are collectively grouped under the acronym of CATCH-22 (cardiac, abnormal facies, thymic hypoplasia, cleft palate, and hypocalcemia resulting from 22q11 deletion).

1. **C**ardiac. The great majority of patients (85%) with the syndrome have serious CHDs. The common ones include TOF (25%), interrupted aortic arch (15%), VSD (15%), persistent truncus arteriosus (9%), and isolated aortic arch anomalies (5%).
2. **A**bnormal facies: hypertelorism, micrognathia, short philtrum with fish-mouth appearance, antimongoloid slant, telecanthus with short palpebral fissures, and low-set ears, often with defective pinna.
3. **T**hymic hypoplasia or aplasia, with mild to moderate decrease in T-cell number.
4. **C**left: anomalies in the palate (70-80%) with speech and feeding disorders.
5. **H**ypocalcemia (60%) is due to hypoparathyroidism.
6. **G**eneral. Short stature, mental retardation, and hypotonia in infancy are frequent. Occasionally, psychiatric disorders (e.g., schizophrenia and bipolar disorder) develop.

Management

1. Correction of cardiac malformation is required; cardiac defects are major causes of early death.
2. Irradiated, cytomegalovirus-negative blood products must be administered because of the risk of graft versus host disease with nonirradiated products.

3. Monitoring of serum calcium levels and supplementation of calcium and vitamin D are important.
 - a. Calcium gluconate (Kalcinate), 500-750 mg/kg/day, PO, QID, or calcium carbonate (Oscal, Titalac, Oystercal, Caltrate), 112.5-162.5 mg/kg/day, given QID.
 - b. Ergocalciferol (vitamin D2), 25,000-200,000 U PO QD.
4. Live vaccines are contraindicated in patients with DiGeorge syndrome and in household members because of the risk of shedding live organisms.
5. Early thymus transplantation may promote successful immune reconstitution.

FRIEDREICH'S ATAXIA

Description

This autosomal recessive disease includes the onset of ataxia usually before age 10 years. Explosive dysarthric speech and nystagmus are characteristic, but intelligence is preserved.

Cardiovascular Manifestations

1. Cardiomyopathy is found in approximately 30% of the cases. Hypertrophic cardiomyopathy with normal LV systolic function is the most common finding. In advanced stage, the LV enlarges, the LV wall thickness decreases, and LV systolic function decreases. CHF is the terminal event, with most patients dying before age 40 years.
2. The ECG may show the T vector change in the limb leads or left precordial leads. Occasionally, LVH, RVH, abnormal Q waves, or short PR intervals are found.

Management

The same as described under cardiomyopathy.

HYPERTHYROIDISM: CONGENITAL AND ACQUIRED

Description

1. Hyperthyroidism results from excess production of T3 (triiodothyronine), T4 (thyroxine), or both. The level of thyroid stimulating hormone (TSH) is suppressed.
2. The actions of thyroid hormone on the CV system include:
 - (1) increasing heart rate, cardiac contractility, and cardiac output;
 - (2) increasing systolic pressure and decreasing diastolic pressure, with mean pressure unchanged; and
 - (3) increasing myocardial sensitivity to catecholamines.

Clinical Manifestations

1. Congenital hyperthyroidism (neonatal Graves disease): an anxious, irritable, and unusually alert baby with widely open eyes (exophthalmic). Many of the infants are premature and most have goiters.

2. Children with juvenile hyperthyroidism (Graves disease) are hyperactive, irritable, and excitable. The patients have exophthalmos and a goiter. There is a 5:1 female to male ratio.
3. Cardiovascular manifestations include tachycardia, full and bounding pulses, and increased systolic and pulse pressures. Bruits may be audible over the enlarged thyroid in children but not in newborns. In severely affected patients, cardiac enlargement and cardiac failure may develop.
4. Chest radiographs usually are normal unless CHF develops.
5. The ECG may show sinus tachycardia, peaked P waves, various arrhythmias (SVT, junctional rhythm), complete heart block, RVH, LVH, or biventricular hypertrophy.
6. Echo studies reveal a hyperkinetic LV with increased fractional shortening.

Management

1. In severely affected patients, a β -adrenergic blocker such as propranolol is indicated to reduce the effect of catecholamines.
2. Treatment of hyperthyroidism with antithyroid drugs: propylthiouracil or methimazole (Tapazole).
3. If CHF develops, anticongestive medications are indicated (see Chapter 19).

HYPOTHYROIDISM: CONGENITAL AND ACQUIRED

Description

1. Congenital type. Clinical signs may not appear until 3 months of age. A protuberant tongue, cool and mottled skin, subnormal temperature, carotenemia, and myxedema are typical. Untreated children become mentally retarded and slow in physical development.
2. Acquired type. It may be caused by lymphocytic thyroiditis (Hashimoto disease or autoimmune thyroiditis), subtotal or complete thyroidectomy, or protracted ingestion of goitrogens, iodides, or cobalt medications. Rarely, amiodarone can cause hypothyroidism. Serum T3 and T4 are low or borderline and TSH is high. Hypercholesterolemia is common.

Cardiovascular Manifestations

1. Significant bradycardia, weak arterial pulse, hypotension, and nonpitting facial and peripheral edema may be present.
2. The ECG abnormalities may include some or all of the following: low QRS voltages, especially in the limb leads; low T wave amplitude; prolongation of PR and QT intervals; and dome-shaped T wave with an absent ST segment ("mosque" sign).
3. Echo studies may show pericardial effusion, hypertrophic cardiomyopathy or asymmetric septal hypertrophy.
4. In congenital type, PDA and PS are frequently found.

Management

1. L-thyroxine given orally is the treatment of choice. Monitor T4 and TSH frequently.
2. In acquired type, treatment of hypercholesterolemia, if present.

INFANTS OF DIABETIC MOTHERS

Description

1. In general, infants of diabetic mothers (IDM) have higher prevalence of congenital malformations of multiple organ systems, occurring at three to four times the rate seen in the general population. Common ones include neural tube defects (anencephaly, myelomeningocele), CHDs (such as ASD, VSD, TGA, tricuspid atresia, COA, etc.), and sacral dysgenesis or agenesis.
2. In addition to the high prevalence of congenital anomalies, IDMs have a high prevalence of cardiomyopathy and persistent pulmonary hypertension of newborn (PPHN).
 - a. Hypertrophic cardiomyopathy (either concentric or asymmetric septal hypertrophy) with or without obstruction is seen in 10% to 20% of the patients.
 - b. An increased risk of PPHN may be due to conditions that promote the persistence of pulmonary hypertension, such as hypoglycemia, perinatal asphyxia, respiratory distress, and polycythemia.

Clinical Findings of Cardiomyopathy

1. Signs of CHF with gallop rhythm may be found in 5% to 10% of these babies.
2. Chest radiographs may show varying degrees of cardiomegaly with normal or increased PVM.
3. The ECG may show a long QT interval (caused by hypocalcemia) and occasional RVH, LVH, or BVH.
4. Echo findings of cardiomyopathy in IDMs may include the following.
 - a. An increase in the LV wall thickness, often with asymmetric septal hypertrophy, and supernormal contractility of the LV.
 - b. Evidence of LVOT obstruction (seen in about 50% of cases).
 - c. Rarely, the LV is dilated with decreased contractility (dilated cardiomyopathy).

Management

1. Hypoglycemia and hypocalcemia should be corrected, if present.
2. In most cases, the hypertrophy spontaneously resolves within the first 6 to 12 months of life. β -Adrenergic blockers, such as propranolol, may help reduce the LVOT obstruction, but treatment usually is not necessary.
3. Digitalis and other inotropic agents are contraindicated because they may worsen the obstruction.
4. If CHF develops, the usual anticongestive measures are indicated.

MARFAN SYNDROME**Description**

Marfan syndrome is a generalized connective tissue disease involving skeletal, cardiovascular, and ocular systems. It is inherited as an autosomal dominant pattern with variable expressivity.

1. Skeletal: tall stature with long slim limbs, arachnodactyly, muscle hypotonia, joint laxity with scoliosis and kyphosis, pectus excavatum or carinatum, and narrow facies.
2. Cardiovascular involvement occurs in 50% by the age of 21 (see next section).
3. Eye manifestations may include lens subluxation, increased axial globe length, myopia, and retinal detachment.

Cardiovascular Involvement

1. The CV abnormalities may include the following.
 - a. Dilatation of the sinus of Valsalva, dilatation of the ascending aorta, and aortic regurgitation (AR) are common.
 - b. Mitral valve abnormalities are more common than aortic lesions in children, including MR and mitral valve prolapse (MVP).
 - c. Aneurysm of the pulmonary artery (PA) is less frequently seen.
 - d. Rarely, rupture of chordae tendineae, aneurysm of the abdominal aorta, and aneurysmal dilatation of the proximal coronary arteries may occur.
2. The ECG may show LVH, T wave inversion in leads II and III, aVF, and left precordial leads, and first-degree AV block.
3. Chest radiographs may show a prominence of the ascending aorta, aortic knob, or main PA segment, and rarely cardiomegaly.
4. Echo studies show:
 - a. Increased dimension of the aortic root with or without AR.
 - b. "Redundant" mitral valve or MVP with thickened valve leaflets and MR.
 - c. In children, adult echo diagnostic criteria of MVP are rarely met, because MVP is a progressive disease. Systolic straightening or convex superior bowing of the leaflets or superior displacement of the mitral coaptation point may be an important sign of early MVP in this age group.
5. Early death is commonly due to aortic dissection, chronic AR, or severe MR.

Management

1. Periodic examination of the aortic root dimension and the status of the MR and MVP is important.
2. β -blockers (atenolol, propranolol) are effective in slowing the rate of aortic dilatation and reducing the development of aortic complications. Thus, β -blockers with or without ACE inhibitors should be administered to children when the aortic root size exceeds the upper limit of normal for age.
3. Discourage certain physical activities, such as weight lifting, rowing, push-ups, pull-ups, sit-ups, and hanging on a monkey bar, which may increase damage to the aortic root and aortic and mitral valves.

4. Surgery should be considered when the diameter of the aortic root increases significantly. However, there is controversy as to what is considered significant enlargement of the aortic root to require surgery. Recently, a maximum sinus dimension of 5 cm or a rapid increase in dimension (> 1 cm/year) have been suggested as indications for surgery (Tweddell et al, 2012). Normal 2D echo dimensions of the aortic root and the aorta are presented in Table D-3, in Appendix D.
5. Valve-sparing aortic root reconstruction appears to be preferable to composite graft surgery.

MUCOPOLYSACCHARIDOSES

Description

1. In mucopolysaccharidoses (MPS), excessive amounts of glycosaminoglycans (previously called mucopolysaccharides) accumulate in various tissues, including the myocardium, cardiac valves, and coronary arteries. Hurler (type IH), Hunter (II), Scheie (IS), Sanfilippo (III), and Morquio (IV) are well-known eponyms.
2. A wide variety of clinical manifestations occur, including growth and mental retardation, skeletal abnormalities, clouded cornea, upper airway obstruction, and cardiac abnormalities (see the following section).
3. In most cases the cause of death is cardiorespiratory failure secondary to cardiac involvement and upper airway obstruction.

Cardiac Manifestations

1. Echo studies show involvement of cardiac valves and myocardium.
 - a. MR is present in about 30% of the patients. It is more frequent in types IH (38%) than other types (24% in type II and 20% in type III). Thickening of the mitral valve is common.
 - b. AR is present in about 15% of the cases, often with thickened aortic valve. It is more common in type II (56%) and type IV (24%).
 - c. Myocardial abnormalities, such as asymmetric septal hypertrophy, hypertrophic cardiomyopathy, dilated cardiomyopathy, and endocardial thickening, are present in about 25% of the cases.
2. The ECG may show a prolonged QTc interval, RVH, LVH, or LAH.
3. Chest radiographs may show cardiomegaly in severe cases of valve regurgitation.

Management

Treatment depends on the abnormalities present.

MUSCULAR DYSTROPHY

Description

1. Duchenne muscular dystrophy (MD), a sex-linked recessive disease, involves the pelvic muscles, and leads to lordosis, waddling gait, and difficulty rising.

2. Becker muscular dystrophy is the same fundamental disease as Duchenne MD but it follows a milder and more protracted course.

Cardiac Involvement

1. Dilated cardiomyopathy is most common. MR and MVP may rarely develop.
2. The ECG abnormalities occur in 90% of the patients. RVH and RBBB are the most common abnormalities. Other abnormalities may include deep Q waves (in V5, V6), short PR interval, and T wave inversion (in the limb leads or V5 and V6).
3. Echo studies show dilated cardiomyopathy in both Duchenne and Becker types. In early stages, only diastolic dysfunction (of reduced diastolic relaxation pattern) may be present. Systolic dysfunction appears later in the disease process.

Management

1. Treatment is the same as that described for dilated cardiomyopathy (see Chapter 11).
2. Recent reports suggest ACE inhibitors (e.g., perindopril) may lead to improved LV function and possible delay of progression of the disease.
3. Addition of carvedilol (0.5-1 mg/kg, twice daily) may have additional benefits. Carvedilol may be added if average heart rate exceeds 100 bpm (on a 24-hr Holter).

MYOTONIC DYSTROPHY

Description

This autosomal dominant disease is characterized by myotonia (increased muscular irritability and contractility with decreased power of relaxation) combined with muscular weakness.

Cardiac Involvement

1. Involvement of the AV conduction and myocardial abnormalities are frequent (due to fatty infiltration).
2. The ECG may show first-degree AV block and intraventricular conduction delay. Second-degree and complete heart block may develop. In addition, atrial fibrillation and flutter and ventricular arrhythmias may develop.
3. Echo studies may show MVP and LV systolic dysfunction with advancing age.
4. Sudden death is frequent, attributable to conduction abnormalities and/or arrhythmias.

Management

1. Patients with symptoms or evidence of arrhythmias should be considered for antiarrhythmic agents and/or pacemaker treatment.
2. LV dysfunction, if present, should be treated.

NOONAN SYNDROME**Description**

1. This autosomal dominant genetic disorder occurs in both males and females. It is associated with normal chromosomes.
2. Characteristic findings include distinctive facial features (large head, wide-spaced eyes, epicanthal folds, low-set ears, and short and broad nose with depressed root), short webbed neck with low posterior hair-line, cubitus valgus, chest deformity (pectus excavatum or carinatum), scoliosis, short stature, and CHD.
3. Although some clinical features are similar to Turner syndrome, the patients with Noonan syndrome are often mentally retarded and normal sexual maturation usually occurs, although delayed.

Cardiovascular Abnormalities

1. Cardiovascular abnormalities are seen in more than 80% of the patients.
2. Pulmonary valve stenosis, often dysplastic, is the most common one (occurring in 25% to 35%). Secundum ASD is often associated with PS.
3. Hypertrophic cardiomyopathy is present in approximately 20% of patients.

Management

1. For significant PS, pulmonary balloon valvuloplasty is initially tried; if unsuccessful, a pulmonary valvectomy or pulmonary homograft may be needed.
2. Hypertrophic cardiomyopathy may be treated with β -blockers or surgical myomectomy.
3. The patients should be followed by endocrinologists for possible need of growth hormone therapy, thyroid hormone replacement, or pubertal induction with estrogen (for females) or testosterone (for males).

RHEUMATOID ARTHRITIS**Description**

The synovium is the principal target of inappropriate immune attack in this condition. Irregular nodular thickening may be seen on cardiac valves (granulomatous valvulitis). Inflammatory cells may infiltrate the myocardium.

Cardiac Involvement

1. Pericarditis is the most common finding (occurring in about 50% of cases). It is most frequent in systemic-onset juvenile rheumatoid arthritis (JRA), occasionally in patients with polyarticular-onset JRA. Small pericardial effusion occurs without symptoms but large effusion may cause chest pain.
2. Myocarditis occurs infrequently (1% to 10%) but can cause CHF and arrhythmias.

3. Rarely, MR and AR with thickening of these valves occurs.
4. Occasionally, LV is dilated with systolic dysfunction.
5. The ECG may show nonspecific ST-T changes (in 20% of cases). Rarely, heart block can occur.

Management

1. Nonsteroidal antiinflammatory agents such as naproxen (15 mg/kg/day in 2 divided doses) may be used for mild pericarditis.
2. For symptomatic or severe pericarditis, corticosteroids are used. Prednisone 0.5-2 mg/kg/day (given TID or QID) for more than 1 week is gradually reduced by approximately 20% each week (given as a single dose).
3. Tamponade is treated with pericardiocentesis.

SYSTEMIC LUPUS ERYTHEMATOSUS

Description

1. Girls over 8 years of age are most commonly affected (78%), with a girls to boys ratio of 6:1.
2. Varying degrees of immune-mediated changes occur in all layers of the heart: pericarditis, myocarditis, and classical verrucous Libman-Sacks lesion (on the cardiac valves).

Cardiovascular Manifestations

1. Pericarditis with pericardial effusion is the most common manifestation (occurring in about 25%) and is often asymptomatic.
2. Myocarditis occurs in 2% to 25%, with resting tachycardia.
3. Echo studies show:
 - a. Irregular vegetations, 2-4 mm in diameter (Libman-Sacks endocarditis), are seen most commonly on the mitral valve and less commonly on the aortic valve.
 - b. Diffuse thickening of the mitral or aortic valve (with or without regurgitation) is a more frequent finding than the verrucous lesion.

Management

1. If active valvulitis is suspected, corticosteroid therapy may be warranted.
2. Anticoagulation therapy should also be considered.

TURNER SYNDROME

Description

1. Standard karyotyping shows 45,X (in more than 50%); others have a combination of monosomy X and normal cells (45,X/46,XX) (mosaic Turner syndrome).
2. Edema of the dorsa of the hands and feet and loose skinfolds at the nape of the neck in a female neonate are characteristic.
3. In childhood, webbing of the neck, broad chest with wide-spaced nipples, cubitus valgus, and small stature are characteristic.

Cardiac Findings

1. Cardiovascular abnormalities are found in about 35% of the patients.
2. Bicuspid aortic valve (BAV), COA, and aortic wall abnormalities (ascending aortic dilatation, aneurysm formation, and aortic dissection) are more commonly found in patients with webbing of the neck.
3. Less common anomalies include elongated transverse arch, PAPVR involving the left upper PV (13%), and persistent left SVC (13%).

Management

1. Cardiac follow-up is required with attention to the following:
 - a. Aortic dimension should be determined on a regular basis (by MRI every 5 to 10 yr). If the aorta is enlarged, treat it with β -blockers.
 - b. Monitor BP for hypertension.
 - c. Exercise restriction. Highly competitive strenuous sports and isometric exercises are not recommended in patients with a dilated aortic root.
2. Follow-up by pediatric endocrinologists for the need of growth hormone and puberty induction with estrogen therapy.
3. Follow-up by an OB/GYN specialist because natural pregnancy occurs in 2% to 5% of the patients. Pregnancy carries a high risk because of possible aortic dissection during pregnancy and the postpartum period. History of surgically repaired CV defect, BAV, aortic dilatation, or systemic hypertension are relative contraindications of pregnancy.

WILLIAMS SYNDROME

Description

A microdeletion in the chromosomal region 7q11.23 near the elastin gene (ELN) is responsible. Elastin is protein that allows blood vessels and other tissues to stretch. Elastin arteriopathy (with stenosis) most commonly affects the ascending aorta and the pulmonary arteries. Males and females are equally affected.

Cardiovascular Pathology

1. Supravalvular aortic stenosis and PA stenosis are the two most common abnormalities (occurring singly or together in 55% to 80%).
2. Less common defects include COA, hypoplastic aortic arch, ASD, VSD, TOF, complete AV canal, and hypertrophic cardiomyopathy.
3. Coronary ostial narrowing and coronary artery stenosis may occur.
4. Rarely renal artery stenosis with hypertension may result.
5. Hypercalcemia is noted in approximately 15% of infants with the syndrome but usually resolves in the first few years of life.
6. Sudden deaths with no apparent instigating event have been reported after the use of anesthesia, after sedation, or during invasive procedures (such as cardiac catheterization and heart surgery).
7. Higher frequency of prolonged QTc interval has been found in patients with the syndrome than in the control group; this has been raised as a possible cause of sudden death. Prolonged QTc interval (≥ 460 ms)

is found in 13.6% of the patients (compared to 2.0% in controls). JTc prolongation (>340 ms) is found in 11.7% of the patients (compared to 1.8% in controls).

Management

1. Annual cardiology evaluation with assessment of the cardiac conditions, measurement of blood pressure, and check of the QTc interval.
2. Hypercalcemia should be treated, if present. Avoid taking extra calcium and vitamin D.
3. When planning a procedure, history should be evaluated carefully for syncope, angina, fatigue or dyspnea, and hemodynamic instability during previous anesthesia or sedation.
4. Avoid medications that are known to prolong the QTc interval.

PART V

ARRHYTHMIAS AND ATRIOVENTRICULAR CONDUCTION DISTURBANCES

This part discusses cardiac arrhythmias, atrioventricular conduction disturbances, cardiac pacemakers, and implantable cardioverter defibrillators (ICD).

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Chapter 16

Cardiac Arrhythmias

Normal heart rate varies with age: the younger the child, the faster the heart rate. Therefore, the definitions used for adults of bradycardia (fewer than 60 beats/min) and tachycardia (above 100 beats/min) have little significance for children. A child has tachycardia when the heart rate is beyond the upper limit of normal for age, and bradycardia when the heart rate is slower than the lower limit of normal (see Table 2-1).

I. RHYTHMS ORIGINATING IN THE SINUS NODE

All rhythms that originate in the sinoatrial (SA) node (sinus rhythm) have two important characteristics.

1. A P wave is present in front of each QRS complex with a regular PR interval. (The PR interval may be prolonged, as in first-degree AV block).
2. The P axis is between 0 and +90 degrees, often a neglected criterion. This produces upright P waves in lead II and inverted P waves in aVR (see Figs. 2-6 and 2-7).

Regular Sinus Rhythm

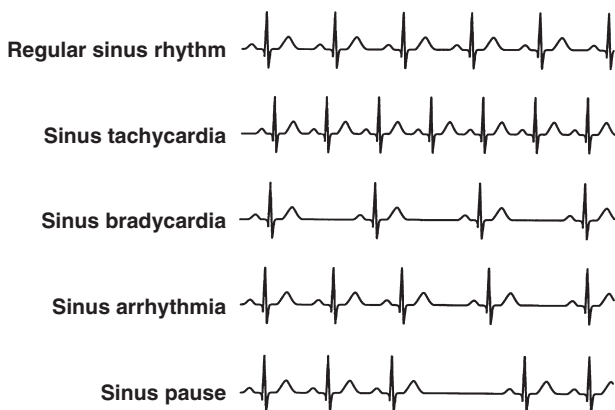
1. **Description:** The rhythm is regular and the rate is normal for age. Two characteristics of sinus rhythm (as described previously) are present (Fig. 16-1).
2. **Significance:** This rhythm is normal at any age.
3. **Treatment:** No treatment is required.

Sinus Tachycardia

1. **Description:** The characteristics of sinus rhythm are present. A rate above 140 beats/min in children and above 170 beats/min in infants may be significant. In sinus tachycardia, the heart rate is usually lower than 200 beats/min (Fig. 16-1).
2. **Causes:** Anxiety, fever, hypovolemia, circulatory shock, anemia, CHF, catecholamines, thyrotoxicosis, and myocardial disease are possible causes.
3. **Significance:** Increased cardiac work is well tolerated by the healthy myocardium.
4. **Treatment:** The underlying cause is treated.

Sinus Bradycardia

1. **Description:** The characteristics of sinus rhythm are present. A rate below 80 beats/min in newborn infants and below 60 beats/min in older children may be significant (Fig. 16-1).

**FIGURE 16-1**

Normal and abnormal rhythms originating in the sinoatrial node. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

2. **Causes:** Sinus bradycardia may occur in trained athletes. Vagal stimulation, increased intracranial pressure, hypothyroidism, hypothermia, hypoxia, and drugs such as digitalis and β -adrenergic blockers are possible causes.
3. **Significance:** Some patients with marked bradycardia do not maintain normal cardiac output.
4. **Treatment:** The underlying cause is treated.

Sinus Arrhythmia

1. **Description:** There is a phasic variation in the heart rate, increasing during inspiration and decreasing during expiration, and the two characteristics of sinus rhythm are maintained (Fig. 16-1).
2. **Causes:** This normal phenomenon is due to a phasic variation in the firing rate of cardiac autonomic nerves with the phase of respiration.
3. **Significance:** There is no hemodynamic significance.
4. **Treatment:** No treatment is indicated.

Sinus Pause

1. **Description:** In *sinus pause*, there is a momentary cessation of sinus node pacemaker activity, resulting in the absence of the P wave and QRS complex for a relatively short duration (see Fig. 16-1). *Sinus arrest* lasts longer and usually results in an escape beat (such as junctional escape beat).
2. **Causes:** Increased vagal tone, hypoxia, digitalis toxicity, and sick sinus syndrome (see next section). Well-conditioned athletes may have bradycardia and sinus pause of greater than 2 seconds due to prominent vagal influence.

3. **Significance:** Sinus pause of less than 2 seconds is normal in young children and adolescents. Sinus pause usually has no hemodynamic significance.
4. **Treatment:** Treatment is rarely indicated except in sick sinus syndrome and digitalis toxicity.

Sinoatrial Exit Block

1. **Description:** A P wave is absent from the normally expected P wave resulting in a long RR interval. The duration of the pause is a multiple of the basic PP interval. An impulse formed within the sinus node fails to propagate normally to the atria.
2. **Causes:** Excessive vagal stimulation, myocarditis or fibrosis involving the atrium, and drugs such as quinidine, procainamide or digitalis
3. **Significance:** It is usually transient and has no hemodynamic significance.
4. **Treatment:** The underlying cause is treated.

Sinus Node Dysfunction (Sick Sinus Syndrome)

1. **Description:** The sinus node fails to function as the dominant pacemaker of the heart or performs abnormally slowly, producing a variety of arrhythmias. The arrhythmias may include profound sinus bradycardia, sinus arrest with junctional (or nodal) escape, and ectopic atrial or nodal rhythm. When these arrhythmias are accompanied by symptoms such as dizziness or syncope, sinus node dysfunction is referred to as sick sinus syndrome. Long-term ECG recording (such as Holter) is usually required in documenting overall heart rate variation and the prevalence of abnormally slow or fast rhythm.
2. **Causes:** Extensive cardiac surgery involving the atria (e.g., the Fontan operation), arteritis, myocarditis, antiarrhythmic drugs, hypothyroidism, CHD (such as sinus venosus ASD, Ebstein anomaly), and occasionally idiopathic occurring in an otherwise normal heart.
3. **Significance:** Bradytachyarrhythmia is the most worrisome rhythm. Profound bradycardia following a period of tachycardia (overdrive suppression) can cause syncope and even death.
4. **Treatment:**
 - a. Severe bradycardia is treated with atropine (0.02-0.04 mg/kg, IV, q2-4 hr) or isoproterenol (0.05-0.5 mcg/kg, IV) or both.
 - b. Temporary transvenous or transesophageal pacing can be used until a permanent pacing system can be implanted.
 - c. Chronic medical treatment with various drugs has not been uniformly successful.
 - d. Permanent pacemaker implantation is the treatment of choice in symptomatic patients. Most patients receive atrial demand pacing. Patients with any degree of AV nodal dysfunction receive dual-chamber pacemakers.

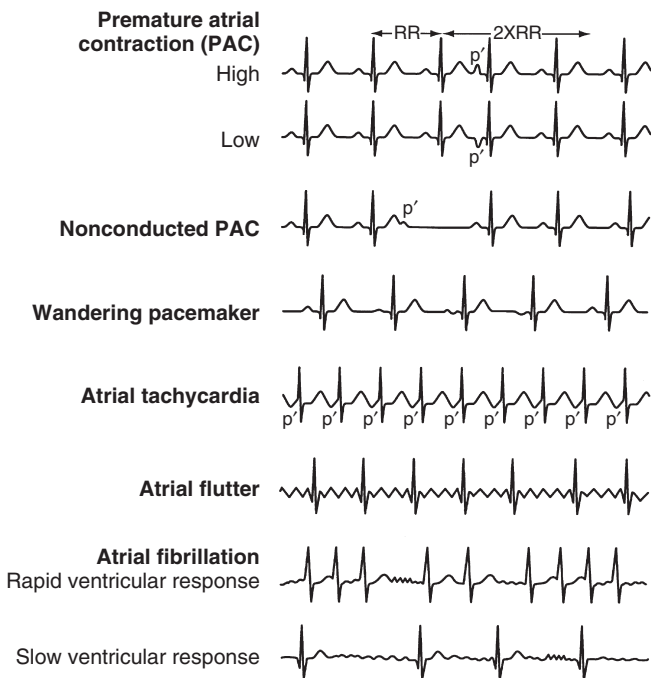
II. RHYTHMS ORIGINATING IN THE ATRIUM

Atrial arrhythmias (Fig. 16-2) are characterized by the following:

1. P waves of unusual contour (abnormal P axis) and/or an abnormal number of P waves per QRS complex.
2. QRS complexes of normal duration (but with occasional wide QRS duration caused by aberrancy).

Premature Atrial Contraction**1. Description**

- a. In PAC the QRS complex occurs prematurely with abnormal P wave morphology. There is an incomplete compensatory pause; i.e., the length of two cycles including one premature beat is less than the length of two normal cycles.
- b. An occasional PAC is not followed by a QRS complex (i.e., a nonconducted PAC) (see Fig. 16-2).

**FIGURE 16-2**

Arrhythmias originating in the atrium. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

- c. A *nonconducted PAC* is differentiated from a second-degree AV block by the prematurity of the nonconducted P wave (P' in Fig. 16-2). The P' wave occurs earlier than the anticipated normal P rate, and the resulting PP' interval is shorter than the normal PP interval for that individual. In second-degree AV block, the P wave that is not followed by the QRS complex occurs at the anticipated time, maintaining a regular PP interval.
2. **Causes:** PAC appears in healthy children, including newborns. It also may appear after cardiac surgery and with digitalis toxicity.
3. **Significance:** There is no hemodynamic significance.
4. **Treatment:** Usually no treatment is indicated except in cases of digitalis toxicity.

Wandering Atrial Pacemaker

1. **Description:** Gradual changes in the shape of P waves and PR intervals occur. The QRS complex is normal (Fig. 16-2).
2. **Causes:** This is seen in otherwise healthy children. It is the result of a gradual shift of impulse formation in the atria through several cardiac cycles.
3. **Significance:** There is no clinical significance.
4. **Treatment:** No treatment is indicated.

Ectopic (or Autonomic) Atrial Tachycardia

1. **Description:**
 - a. There is a narrow QRS complex tachycardia (in the absence of aberrancy or preexisting bundle branch block) with visible P waves at an inappropriately rapid rate.
 - b. The P axis is different from that of sinus rhythm (Fig. 16-2). When the ectopic focus is near the sinus node, the P axis may be the same as in sinus rhythm.
 - c. The usual heart rate in older children is between 110 and 160 beats/min, but the tachycardia rate varies substantially during the course of a day, reaching 200 beats/min with sympathetic stimuli. Holter monitoring may demonstrate a characteristic gradual acceleration of the heart rate, the so called "warming up" period, rather than abrupt onset and termination seen with re-entrant AV tachycardia.
 - d. It represents about 20% of supraventricular tachycardia (SVT). This arrhythmia is sometimes difficult to distinguish from the re-entrant AV tachycardia and thus it is included under "supraventricular tachycardia."
2. **Causes:** This arrhythmia originates from a single focus in the atrium. It is believed to be secondary to increased automaticity of nonsinus atrial focus or foci. Myocarditis, cardiomyopathies, atrial dilatation, atrial tumors, and previous cardiac surgery involving atria (such as Fontan procedure) may be the cause. Most patients have a structurally normal heart (idiopathic).

3. **Significance:** CHF is common with chronic cases. There is a high association with tachycardia-induced cardiomyopathy.
4. **Treatment:** It is refractory to medical therapy and cardioversion.
 - a. Drugs that are effective in re-entrant atrial tachycardia (such as adenosine) do not terminate the tachycardia. Cardioversion is ineffective because the ectopic rhythm resumes immediately.
 - b. The goal may be to slow the ventricular rate (using digoxin or β -blockers) rather than to try to convert the arrhythmia to sinus rhythm.
 - c. Intravenous amiodarone may achieve rate control relatively quickly.
 - d. Long-term oral antiarrhythmic drugs (such as flecainide or amiodarone) are the mainstay of therapy in patients not undergoing radiofrequency ablation.
 - e. Radiofrequency ablation may prove to be effective in nearly 90% of cases. In children, the foci are found in the LA near the pulmonary veins and the atrial appendage (in contrast to the RA found in adults).

Multifocal (or Chaotic) Atrial Tachycardia

1. **Description:** There are three or more distinct P wave morphologies. The PP and RR intervals are irregular with variable PR intervals. The arrhythmia may be misdiagnosed as atrial fibrillation.
2. **Causes:** Most patients with the condition are infants; it is very rare after 5 years of age. Thirty percent to 50% have respiratory illness. Myocarditis and birth asphyxia have been described. This arrhythmia may occur with or without CHDs. The mechanism of this arrhythmia has been poorly defined.
3. **Significance:** CHF may develop. Sudden death has been reported in up to 17% while on therapy. Long duration of the arrhythmia may cause LV systolic dysfunction. Spontaneous resolution frequently occurs.
4. **Treatment:**
 - a. Adenosine is ineffective in terminating the tachycardia (a useful diagnostic sign of the condition). This arrhythmia is also refractory to cardiac pacing and cardioversion.
 - b. Drugs that slow AV conduction (propranolol or digoxin) and those that decrease automaticity (such as class IA or IC or class III) may be useful.
 - c. Amiodarone (IV followed by PO) appears to be the current treatment of choice.

Atrial Flutter

1. **Description:** Atrial flutter is characterized by a fast atrial rate (F waves with saw-tooth configuration) of about 300 (ranges 240 to 360) beats/min, the ventricle responding with varying degrees of block (e.g., 2:1, 3:1, 4:1), and normal QRS complexes (see Fig. 16-2).
2. **Causes:** Structural heart disease with dilated atria, myocarditis, thyrotoxicosis, and previous surgery involving atria (such as Senning or Fontan operation) are possible causes. However, most fetuses and neonates with atrial flutter have a normal heart.

3. **Significance:** The ventricular rate determines the eventual cardiac output; a too-rapid ventricular rate may decrease the cardiac output. Thrombus formation may lead to embolic events. Uncontrolled atrial flutter may precipitate heart failure.
4. **Treatment:**
 - a. In acute situations, synchronized cardioversion is the treatment of choice. Adenosine is not effective.
 - b. For long-standing atrial flutter or fibrillation (of 24 to 48 hours) or those with unknown duration, it is important to rule out intracardiac thrombus by echo (preferably transesophageal echo) before cardioversion because it may lead to cerebral embolization. If a thrombus is found or suspected, anticoagulation with warfarin (with INR 2-3) is started and cardioversion delayed for 2-3 weeks. After conversion to sinus rhythm, warfarin is continued for an additional 3 to 4 weeks.
 - c. For control of the ventricular rate, calcium channel blockers, propranolol, or digoxin may be used.
 - d. For prevention of recurrence, class I (quinidine) and class III (amiodarone) antiarrhythmic agents may be effective in some cases.
 - e. For refractory cases, antitachycardia pacing or radiofrequency ablation may be indicated.

Atrial Fibrillation

1. **Description:** Atrial fibrillation is characterized by an extremely fast atrial rate (f wave at 350 to 600 beats/min) and an irregular ventricular response with narrow QRS complexes (see Fig. 16-2).
2. **Causes:** Same as those for atrial flutter.
3. **Significance:** Atrial fibrillation usually suggests a significant pathology. Rapid ventricular rate and the loss of coordinated contraction of the atria and ventricles decrease cardiac output. Atrial thrombus formation is quite common.
4. **Treatment:** Treatment of atrial fibrillation is similar to that described under atrial flutter.
 - a. If atrial fibrillation has been present more than 48 hours, the patient should receive anticoagulation with warfarin for 3 to 4 weeks to prevent systemic embolization of atrial thrombus, if the conversion can be delayed. Anticoagulation is continued for 4 weeks after restoration of sinus rhythm. If cardioversion cannot be delayed, heparin should be started, and cardioversion performed when activated partial thromboplastin time (aPTT) reaches 1.5 to 2.5 times control (in 5 to 10 days), with subsequent oral anticoagulation with warfarin.
 - b. Propranolol or digoxin may be used to slow the ventricular rate.
 - c. Class I antiarrhythmic agents (e.g., quinidine, procainamide, flecainide) and the class III agent amiodarone may be used but the success rate in rhythm conversion is disappointingly low. These agents may prevent recurrence.

- d. In patients with chronic atrial fibrillation, anticoagulation with warfarin should be used to reduce the incidence of thromboembolism.
- e. In the Cox maze procedure (or the “cut-and-sew-maze”), multiple surgical incisions are made in the right and left atria that are then repaired in an attempt to minimize the formation of a re-entrant loop. The procedure showed greater than a 96% cure rate 10 years after the surgery in adult patients.
- f. Radiofrequency ablation to electrically isolate the pulmonary veins from the left atrium or directly ablating the ectopic focus within the pulmonary veins has shown better results than pharmacologic agents in rhythm control in adults. Stenosis of the pulmonary vein(s) is a significant complication of the procedure.

III. RHYTHMS ORIGINATING IN THE AV NODE

Rhythms originating in the AV node (Fig. 16-3) are characterized by the following:

1. The P wave may be absent, or inverted P waves may follow the QRS complex.
2. The QRS complex is usually normal in duration and configuration.

Junctional rhythm describes an abnormal heart rhythm resulting from impulses coming from a locus of tissue in the area of the atrioventricular (AV) node, the “junction” between atria and ventricles. Since the NH region of the AV node is the only part of the AV node with demonstrable ability to pace the heart, some authorities prefer the term “nodal” over “junctional.”

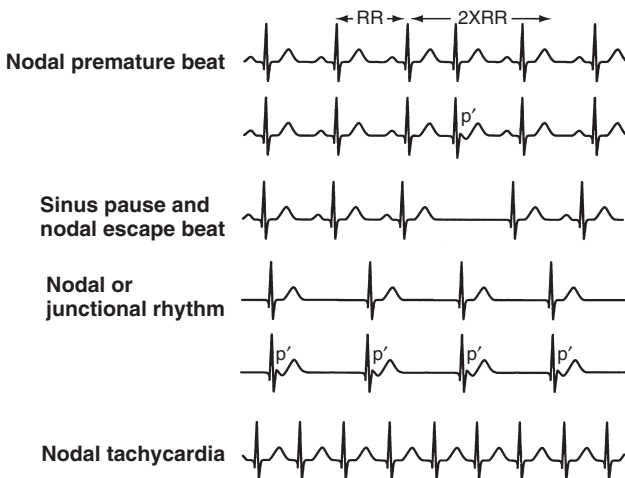


FIGURE 16-3

Arrhythmias originating in the atrioventricular node. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

Junctional (or Nodal) Premature Beats

1. **Description:** A normal QRS complex occurs prematurely. P waves are usually absent, but inverted P waves may follow QRS complexes. The compensatory pause may be complete or incomplete (see Fig. 16-3).
2. **Causes:** Usually idiopathic in an otherwise normal heart but may result from cardiac surgery or digitalis toxicity.
3. **Significance:** Usually no hemodynamic significance.
4. **Treatment:** Treatment is not indicated unless caused by digitalis toxicity.

Junctional (or Nodal) Escape Beat

1. **Description:** When the sinus node impulse fails to reach the AV node, the node-His (NH) region of the AV node will initiate an impulse (nodal or junctional escape beat). The QRS complex occurs later than the anticipated normal beat. The P wave may be absent (see Fig. 16-3), or an inverted P wave may follow the QRS complex.
2. **Causes:** It may follow cardiac surgery involving the atria (e.g., the Fontan operation) or may be seen in otherwise healthy children.
3. **Significance:** Little hemodynamic significance.
4. **Treatment:** Generally no specific treatment is required.

Junctional (or Nodal) Rhythm

1. **Description:** If there is a persistent failure of the sinus node, the AV node may function as the main pacemaker of the heart with a relatively slow rate (40 to 60 beats/min). P waves are absent or inverted P waves follow QRS complexes (see Fig. 16-3).
2. **Causes:** It may be seen in an otherwise normal heart, after cardiac surgery, in conditions of an increased vagal tone (e.g., increased intracranial pressure, pharyngeal stimulation), and with digitalis toxicity. Rarely, it may be seen in children with polysplenia syndrome.
3. **Significance:** The slow heart rate may significantly decrease the cardiac output and produce symptoms.
4. **Treatment:** No treatment is indicated if the patient is asymptomatic. Atropine or electric pacing is indicated for symptoms. Treatment is directed to digitalis toxicity if caused by digitalis.

Accelerated Junctional (or Nodal) Rhythm

1. **Description:** In the presence of normal sinus rate and AV conduction, if the AV node (NH region) with enhanced automaticity captures the pacemaker function (60 to 120 beats/min), the rhythm is called accelerated nodal (or AV junctional) rhythm. P waves are absent or inverted P waves follow the normal QRS complexes.
2. **Causes:** Idiopathic, digitalis toxicity, myocarditis, or previous cardiac surgery.
3. **Significance:** Little hemodynamic significance.
4. **Treatment:** No treatment is necessary unless caused by digitalis toxicity.

Junctional Ectopic Tachycardia (Nodal Tachycardia)

1. **Description:** The ventricular rates vary from 120 to 200 beats/min. P waves are absent (Fig. 16-3) or inverted P waves follow the QRS complexes. The QRS complex is usually normal, but aberration may occur. Junctional tachycardia is difficult to separate from other types of SVT. Therefore, the arrhythmia is grouped under SVT.
2. **Causes:** Enhanced automaticity of the junctional area is the suspected mechanism. There are two types: postoperative and congenital.
 - a. The postoperative type is more common than the congenital type. This transient disorder is seen after open heart surgery, and lasts 24 to 48 hours. Trauma, stretch, or ischemia to the AV node and electrolyte imbalance may be responsible for the rhythm disorder.
 - b. The rare congenital type may occur with or without associated CHDs.
3. **Significance:**
 - a. In the postoperative type, a loss of atrioventricular synchrony in the presence of a fast rate (nearly 200 beats/min) compromises cardiac output, leading to a fall in BP. Increased endogenous catecholamine levels and administered inotropic support (to maintain adequate BP and renal perfusion) may result in peripheral vasoconstriction leading to a rise in the core temperature. The rising core temperature exacerbates the tachycardia, worsening ventricular performance.
 - b. In the congenital form, most patients present before 6 months of age, usually with CHF (with overall mortality rate of 35%).
4. **Treatment:**
 - a. For the postoperative type: Heart rate <170 beats/min is well tolerated but rates >170-190 beats/min need to be slowed.
 - (1) Atrial overdrive pacing (typically 10 beats/min higher than the rate) often restores atrioventricular synchrony.
 - (2) Mild systemic hypothermia is induced, usually a core temperature of 34° C to 35° C. At a core temperature below 32° C, ventricular function may be impaired.
 - (3) Cardiac output is maximized by carefully titrating fluid and electrolyte balance, inotropic support, and pain management.
 - (4) Intravenous amiodarone appears to be the drug of choice as antiarrhythmic therapy. In the past, procainamide IV drip was widely used with good success. Digoxin is no longer used in this situation.
 - (5) ECMO can be used as an alternative in selected patients.
 - b. For the congenital type, amiodarone appears to be the drug of choice. Amiodarone in high dose was effective in 85% of the patients with almost 75% survival rate. If amiodarone is not effective, ablation therapy may be tried.

IV. SUPRAVENTRICULAR TACHYCARDIA

Supraventricular tachycardia (SVT) refers to any rapid heart rhythm originating above the ventricular tissue, including atrial and junctional tachycardias. SVTs are caused by two mechanisms: re-entry and automaticity.

1. Re-entry: Most cases of SVTs are due to re-entrant (or reciprocating) AV tachycardia. This section will discuss only re-entrant (or reciprocating) AV tachycardia.
2. Automaticity: SVTs caused by increased automaticity of a single focus in the atria or the AV node are infrequent. Examples of this entity include atrial ectopic tachycardia and junctional (or nodal) ectopic tachycardia (which are discussed in other sections).

Re-entrant (or Reciprocating) AV Tachycardia

Classification and Mechanism of Re-entry AV Tachycardia

1. In SVT due to re-entry, two pathways are involved; one is the AV node and the other is an accessory pathway.
 - a. The accessory pathway may be an anatomically separate bypass tract such as the bundle of Kent, which produces accessory re-entrant (or reciprocating) AV tachycardia (accessory RAVT). After conversion to sinus rhythm, the ECG will show WPW preexcitation.
 - b. The nodal pathway is only functionally separate, as in a dual AV node pathway, which produces nodal re-entrant (or reciprocating) AV tachycardia (nodal RAVT). This entity is more common than accessory bundles. After conversion to sinus rhythm, the ECG will not show WPW preexcitation.
2. **Figure 16-4** shows the mechanism of reciprocating AV tachycardias in relation to ECG findings. The left two mechanisms use the

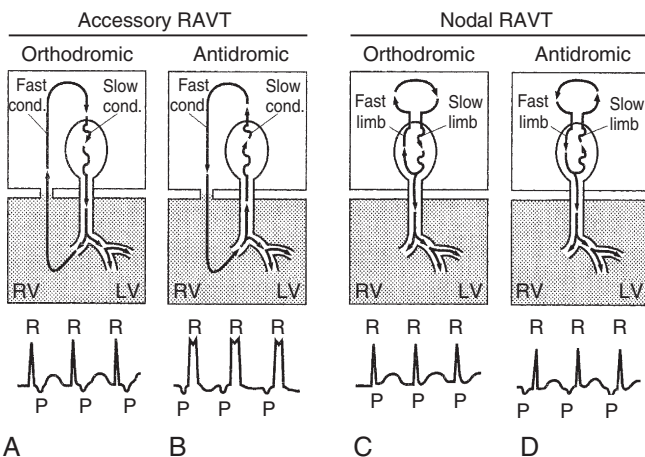


FIGURE 16-4

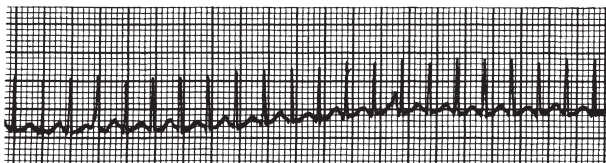
Diagram showing the mechanism of re-entrant (or reciprocating) atrioventricular tachycardia (RAVT) in relation to ECG findings. **A**, Orthodromic accessory re-entrant atrioventricular tachycardia (RAVT); **B**, Antidromic accessory RAVT; **C**, Orthodromic nodal RAVT; **D**, Antidromic nodal RAVT. See text for explanation. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

accessory pathway and the right two mechanisms use the AV node (*nodal*).

3. Brief descriptions of the four subtypes of re-entrant AV tachycardia follow.
 - a. **Accessory RAVT.** Depending on the direction of the conduction through the AV node, two subtypes are present: orthodromic and antidromic accessory RAVTs (see left panel of [Fig. 16-4](#)).
 - (1) Orthodromic ARAVT. A premature atrial contraction (PAC) could initiate the arrhythmia. The PAC may find the accessory bundle refractory, but the AV node may conduct (antegradely), producing a narrow QRS complex. When the impulse reaches the bundle of Kent from the ventricular side, the bundle will have recovered and allows re-entry into the atrium, producing a superiorly directed P wave that is difficult to detect. In turn, the cycle is maintained by re-entry into the AV node, with a very fast heart rate (see [Fig. 16-4, A](#)).
 - (2) Antidromic ARAVT. Less common is a widened QRS complex with antegrade conduction into the ventricle via the accessory (fast) pathway and retrograde conduction through the (slower) AV node (see [Fig. 16-4, B](#)). A premature ventricular contraction (PVC) could initiate this arrhythmia if the recovery time of the two limbs is ideal for the initiation of the reentry.
 - b. **Nodal RAVT.** For this type of SVT to occur, the two pathways in the AV node would have to have, at least temporarily, different conduction and recovery rates, creating the substrate for a re-entry tachycardia. Depending on the direction of the conduction of the slow limb in the AV node, two subtypes are present (right panel of [Fig. 16-4](#)).
 - (1) Orthodromic nodal RAVT. When the normal, slow pathway through the AV node is used in antegrade conduction to the bundle of His, the resulting QRS complex is normal with an abnormal P vector, but the latter is unrecognizable because it is superimposed on the QRS complex (see [Fig. 16-4, C](#)). The resulting tachycardia could be the same as that seen with SVT associated with WPW syndrome. The two can be differentiated only after conversion from the SVT.
 - (2) Antidromic nodal RAVT. In this subtype (see [Fig. 16-4, D](#)), which is uncommon, the fast tract of the AV node transmits the antegrade impulse to the bundle of His, and the normal, slow pathway of the AV node transmits the impulse retrogradely. The resulting SVT demonstrates normal QRS duration, a short PR interval, and an inverted P wave (with the ECG similar to ectopic atrial tachycardia).

Description

1. The heart rate is extremely rapid and regular (usually 240 ± 40 beats/min) (see [Fig. 16-5](#)). The P wave is usually invisible, but when it is visible, it has an abnormal P axis and either precedes or follows the QRS complex. The QRS duration is usually normal, but occasionally aberrancy will prolong the QRS, making differentiation of this arrhythmia from ventricular tachycardia difficult. It used to be called paroxysmal atrial tachycardia (PAT) because its onset and termination were characteristically abrupt.

**FIGURE 16-5**

Rhythm strip of SVT. The heart rate is 300 beats/min. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, 2006, Mosby.)

2. Some characteristics of accessory and nodal RAVTs are as follows.
 - a. Nodal RAVT is more influenced by increased sympathetic tone than accessory RAVT. Thus, it is more likely triggered by physical activity, emotional stress, or abrupt changes in body position.
 - b. Nodal RAVT is less likely to be incessant (and therefore rarely causes tachycardia-induced cardiomyopathy).
 - c. Age of onset.
 - (1) SVT seen in the first year of life is more likely to have accessory RAVT.
 - (2) An adolescent who first has SVT is more likely to have nodal RAVT.
3. Any type of AV block is incompatible with re-entrant tachycardia; AV block would abruptly terminate the tachycardia, at least temporarily. This is why adenosine, which transiently blocks AV conduction, works well for this type of arrhythmia.

Causes

1. No heart disease is found in about 50% of patients.
2. WPW preexcitation is present in 10% to 20% of cases, which is evident only after conversion to sinus rhythm.
3. Some CHDs (e.g., Ebstein anomaly, single ventricle, L-TGA) are more prone to this arrhythmia.
4. SVT may occur following cardiac surgeries.

Significance

1. It may decrease cardiac output and result in CHF in infants (with irritability, tachypnea, poor feeding, and pallor). When CHF develops, the infant's condition can deteriorate rapidly.
2. Older children and adults may present with a fairly unique complaint of "pounding sensation" in the neck, probably caused by cannon waves when the atrium contracts against a simultaneously contracting ventricle.

Treatment

1. Vagal stimulatory maneuvers (e.g., carotid sinus massage, gagging, and pressure on an eyeball) may be effective in older children, but they

are rarely effective in infants. Placing an ice bag on the face (up to 10 seconds) is often successful in infants (by diving reflex). In children, a headstand often successfully interrupts the SVT.

2. Adenosine is considered the drug of choice. It has negative chronotropic, dromotropic, and inotropic actions with a very short duration of action (half-life <10 seconds) and minimal hemodynamic consequences. Adenosine is effective for almost all reciprocating SVT (in which the AV node forms part of the re-entry circuit) and for both narrow- and wide-complex *regular* tachycardia. It is not effective for irregular tachycardia or for nonreciprocating atrial tachycardia, atrial flutter/fibrillation, and ventricular tachycardia. Adenosine is given by rapid intravenous bolus followed by a saline flush, starting at 50 mcg/kg, increasing in increment of 50 mcg/kg, every 1 to 2 min. The usual effective dose is 100-150 mcg/kg with maximum dose of 250 mcg/kg.
3. If the infant is in severe CHF, an immediate cardioversion may be carried out. The initial dose of 0.5 joule/kg is increased in steps up to 2 joule/kg. Alternatively, in infants in CHF, one may start with digoxin (to treat CHF) but, if WPW preexcitation is found, digoxin should be switched to propranolol when the infant's heart failure improves. Verapamil can also be used but it should be used with caution in patients with poor LV function and in young infants.
4. Intravenous administration of propranolol is usually successful in treating SVT in the presence of WPW syndrome. Intravenous verapamil should be avoided in infants younger than 12 months of age because it may produce extreme bradycardia and hypotension.
5. Overdrive suppression (by transesophageal pacing or by atrial pacing) may be effective in children who have been digitalized.
6. For prevention of recurrence of SVT, the following may be used:
 - a. In infants without WPW preexcitation, oral propranolol for 12 months is effective. In children beyond infancy, verapamil can also be used. Digoxin, although occasionally used, is less effective.
 - b. In infants or children with WPW preexcitation on the ECG, propranolol or atenolol is used in long-term management. In the presence of WPW preexcitation, digoxin or verapamil may increase the rate of antegrade conduction of the impulse through the accessory pathway, and therefore should be avoided.
 - c. For children who have infrequent episodes of SVT that result in little hemodynamic compromise, observation is reasonable. They should be taught how to apply vagal maneuvers (such as gagging, headstands).
 - d. In adolescent patients, catheter ablation may be an effective alternative to long-term drug therapy. Ablation therapy is controversial for asymptomatic patients with WPW preexcitation. Ablation is not recommended in infants 1-2 years of age because of a possibility of spontaneous resolution of SVT. Risk of complication is 3% to 4%, including heart block.

V. RHYTHMS ORIGINATING IN THE VENTRICLE

Ventricular arrhythmias (Fig. 16-6) are characterized by the following:

1. Bizarre and wide QRS complexes with T waves pointing in the opposite directions.
2. QRS complexes randomly related to P waves, if visible.

Premature Ventricular Contraction

Description

1. A bizarre, wide QRS complex appears earlier than anticipated, and the T wave points in the opposite direction. A full compensatory pause usually appears; that is, the length of two cycles, including the premature beat, is the same as that of two normal cycles (see Fig. 16-6).
2. PVCs may be classified into several types, depending on their interrelationship, similarities, timing, and coupling intervals.
 - a. By interrelationship of PVCs
 - (1) Ventricular *bigeminy* or *coupling*: each abnormal QRS complex alternates with a normal QRS complex regularly.
 - (2) Ventricular *trigeminy*: each abnormal QRS complex follows two normal QRS complexes regularly.
 - (3) *Couplets*: Two abnormal QRS complexes come in sequence.
 - (4) *Triplets*: Three abnormal QRS complexes come in sequence. Three or more successive PVCs arbitrarily are termed ventricular tachycardia.
 - b. By similarity among abnormal QRS complexes
 - (1) Uniform (monomorphic or unifocal) PVCs: Abnormal QRS complexes have the same configuration in a single lead. It is assumed that they originate from a single focus.
 - (2) Multiform (polymorphic or multifocal) PVCs: Abnormal QRS complexes have different configurations in a single lead. It is assumed that they originate from different foci.
 - c. Coupling interval
 - (1) Fixed coupling. PVCs appear at a constant interval after the QRS complex of the previous cardiac cycle. This suggests ventricular

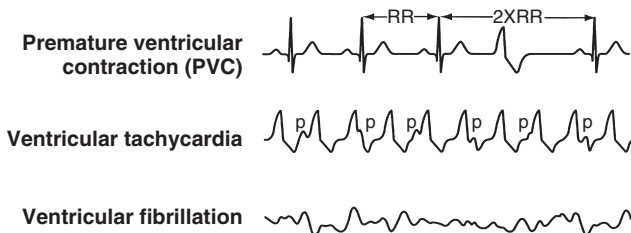


FIGURE 16-6

Ventricular arrhythmias. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

re-entry within the Purkinje system as the underlying mechanism. Most PVCs in children have a fixed coupling interval and a uniform LBBB morphology.

- (2). Varying coupling. When coupling intervals vary by more than 80 msec, the PVCs may result from parasystole. If the intervals between ectopic beats can be factored so that each interval is a multiple of a single basic interval (within 0.08 second), ventricular parasystole is diagnosed. (Ventricular parasystole consists of an impulse-forming focus in the ventricle that is independent of the sinus node-generated impulse and is protected from depolarization by sinus impulses [entrance block].)

Causes

1. PVCs may be seen in otherwise healthy children. Up to 50% to 70% of normal children may show PVCs on 24-hour Holter monitoring.
2. Myocarditis, myocardial injury or infarction, cardiomyopathy (dilated or hypertrophic), cardiac tumors, false tendon, and mitral valve prolapse are possible causes.
3. Arrhythmogenic right ventricular dysplasia (RV cardiomyopathy), long QT syndrome, and Brugada syndrome may cause PVCs.
4. Congenital or acquired heart disease, preoperative or postoperative.
5. Drugs such as catecholamines, theophylline, caffeine, amphetamines, digitalis toxicity, and some anesthetic agents are possible causes.

Significance

1. Occasional PVCs are benign in children, particularly if they are uniform and disappear or decrease in frequency with exercise.
2. PVCs are more likely to be significant if:
 - a. They are associated with underlying heart disease (e.g., preoperative or postoperative status, MVP, cardiomyopathy).
 - b. There is a history of syncope or a family history of sudden death.
 - c. They are precipitated by or increase in frequency with activity.
 - d. They are multiform, particularly couplets.
 - e. There are runs of PVC with symptoms.
 - f. There are incessant or frequent episodes of paroxysmal ventricular tachycardia.

Management

1. Some or all of the following tools are used in the investigation of PVCs and other ventricular arrhythmias:
 - a. ECGs are used to detect QTc prolongation or ST-T changes.
 - b. Echo studies detect structural heart disease or functional abnormalities.
 - c. 24-hour Holter monitoring or event recorder detects the frequency and severity of the arrhythmia.
 - d. Exercise stress testing: Arrhythmias that are potentially related to exercise are significant and require documentation of the relationship.

The induction or exacerbation of arrhythmia with exercise may be an indication of underlying heart disease. In children, PVCs characteristically are reduced or eliminated by exercise.

- e. Cardiac catheterization and/or cardiac MRI, if arrhythmogenic RV dysplasia is suspected.
- f. Electrophysiologic studies and endomyocardial biopsy.
2. In children with otherwise normal hearts, occasional isolated uniform PVCs that are suppressed by exercise do not require extensive investigation or treatment. ECG, echo studies, and 24-hour Holter monitoring suffice.
3. Asymptomatic children with multiform PVCs and ventricular couplets should have 24-hour Holter monitoring, even if they have structurally normal hearts, to detect the severity and extent of ventricular arrhythmias.
4. Children with uniform PVCs, including ventricular bigeminy and trigeminy, do not need to be treated if the echo and exercise stress tests are normal.
5. All children with symptomatic ventricular arrhythmias and those with complex PVCs (multiform PVCs, ventricular couplets, unsustained ventricular tachycardia) should be treated.
 - a. β -blockers (such as atenolol, 1 to 2 mg/kg orally in a single daily dose) are effective for cardiomyopathy and occasionally for RV dysplasia.
 - b. Other antiarrhythmic drugs, such as mexiletine, may be effective.
 - c. Antiarrhythmic agents that prolong the QT interval, such as those of class IA (quinidine, procainamide), class IC (encainide, flecainide), and class III (amiodarone, bretylium), should be avoided.
6. For patients with symptomatic ventricular arrhythmias or sustained ventricular tachycardia and seemingly normal hearts, MRI (preferable) or cardiac catheterization may be indicated to investigate for RV dysplasia. Occasionally, invasive electrophysiologic studies and RV endomyocardial biopsy may be indicated.
7. Children with multiform PVCs and runs of PVCs (ventricular tachycardia) with or without symptoms need to be evaluated by an electrophysiologist.

Accelerated Ventricular Rhythm (AVR)

1. **Description:** There is a wide QRS complex rhythm of short duration (usually several beats but can be longer than 100 beats). The QRS morphology is LBBB pattern in the great majority. The ventricular rate approximates the patient's sinus rate, within $\pm 10\%$ to 15% of the sinus rate (*isochronicity*). The isochronicity with sinus rhythm is more important than the rate per minute. The ventricular rate is usually ≤ 120 beats/min in children and 140-180 beats/min in newborns.
2. **Causes:** AVR is usually an isolated finding. Rarely, it may be associated with underlying heart disease, such as CHD, myocarditis, digitalis toxicity, hypertension, cardiomyopathy, metabolic abnormalities, postoperative state, or MI (in adults). The mechanism of AVR is unknown: ectopic ventricular focus may accelerate its rate enough to overcome sinus rate.

3. **Significance:** Usually asymptomatic and hemodynamically insignificant. Exertional sinus tachycardia usually converts it to sinus rhythm. Rarely seen in patients with syncope, presyncope, or palpitation or found in routine ECG or Holter monitoring
4. **Treatment:** In children, AVR is generally considered benign. AVR is notably resistant to antiarrhythmic agents (no treatment is required).

Ventricular Tachycardia

Description

1. VT is a series of three or more PVCs with a heart rate of 120 to 200 beats/min. QRS complexes are wide and bizarre, with T waves pointing in opposite directions.
2. By duration, VT may be classified as (1) a salvo of VT—a few beats in a row; (2) nonsustained VT—duration of less than 30 seconds; (3) sustained VT—longer than 30 seconds; and (4) incessant VT—refers to lengthy sustained VT that dominates the cardiac rhythm.
3. By morphology, VT may be classified as (1) monomorphic, referring to one dominant QRS form; (b) polymorphic, referring to a beat-to-beat change in the QRS shape; or (3) bidirectional, which is a specific form of polymorphic VT in which the QRS axis shifts across the baseline.
4. Torsades de pointes (meaning “twisting of the points”) is a distinct form of polymorphic VT characterized by a paroxysm of VT during which there are progressive changes in the amplitude and polarity of QRS complexes separated by a narrow transition QRS complex. They occur in patients with marked QT prolongation.
5. VT is sometimes difficult to differentiate from SVT with aberrant conduction. However, wide QRS tachycardia in an infant or child must be considered VT until proven otherwise.

Causes

1. Structural heart diseases (such as TOF, AS, cardiomyopathies, or MVP).
2. Postoperative CHDs (such as TOF, D-TGA, or DORV).
3. Myocarditis, Chagas disease (trypanosomiasis, in South America), myocardial tumors, myocardial ischemia or MI, and pulmonary hypertension.
4. Genetic disorders, such as Brugada syndrome or arrhythmogenic RV dysplasia.
5. Torsades de pointes may be seen in patients with long QT syndrome. A partial list of drugs that may prolong the QT interval is shown in [Box 16-1](#). Classes IA, IC, and III antiarrhythmic drugs prolong the QTc interval but classes II and IV agents do not.
6. Metabolic causes (hypoxia, acidosis, hyperkalemia, hypokalemia, and hypomagnesemia).
7. Mechanical irritation—intraventricular catheter.

BOX 16-1**ACQUIRED CAUSES OF QT PROLONGATION****DRUGS**

Antibiotics: erythromycin, clarithromycin, telithromycin, azithromycin, trimethoprim-sulfamethoxazole

Antifungal agents: fluconazole, itraconazole, ketoconazole

Antiprotozoal agents: pentamidine isethionate

Antihistamines: astemizole, terfenadine (Seldane) (Seldane has been removed from the market for this reason)

Antidepressants: tricyclics such as imipramine (Tofranil), amitriptyline (Elavil), desipramine (Norpramin), and doxepin (Sinequan)

Antipsychotics: haloperidol, risperidone, phenothiazines such as thioridazine (Mellaril) and chlorpromazine (Thorazine)

Antiarrhythmic agents

Class 1A (sodium channel blockers): quinidine, procainamide, disopyramide

Class III (prolong depolarization): amiodarone (rare), bretylium, dofetilide, N-acetyl-procainamide, sotalol

Lipid-lowering agents: probucol

Antianginals: bepridil

Diuretics (through K loss): furosemide (Lasix), ethacrynic acid (Edecrine)

Oral hypoglycemic agents: glibenclamide, glyburide

Organophosphate insecticides

Promotility agents: cisapride

Vasodilators: prenylamine

ELECTROLYTE DISTURBANCES

Hypokalemia: diuretics, hyperventilation

Hypocalcemia

Hypomagnesemia

UNDERLYING MEDICAL CONDITIONS

Bradycardia: complete atrioventricular block, severe bradycardia, sick sinus syndrome

Myocardial dysfunction: anthracycline cardiotoxicity, congestive heart failure, myocarditis, cardiac tumors

Endocrinopathy: hyperparathyroidism, hypothyroidism, pheochromocytoma

Neurologic: encephalitis, head trauma, stroke, subarachnoid hemorrhage

Nutritional: alcoholism, anorexia nervosa, starvation

A more exhaustive updated list of medications that can prolong QTc interval is available at the University of Arizona Center for Education and Research on Therapeutics website (www.torsades.org) or www.qtdrugs.org.

8. Pharmacologic or chemical causes (catecholamine infusion, digitalis toxicity, cocaine, and organophosphate insecticides). Most antiarrhythmic drugs (especially classes IA, IC, and III) are also proarrhythmic.
9. Benign VT may occur in healthy children who have structurally and functionally normal hearts. This group is discussed under a separate heading (see following).

Significance

1. VT usually signifies a serious myocardial pathology or dysfunction and can cause sudden death. Cardiac output may decrease notably and may deteriorate to ventricular fibrillation.
2. Patients may present with dizziness, syncope, palpitation, or chest pain.

Management

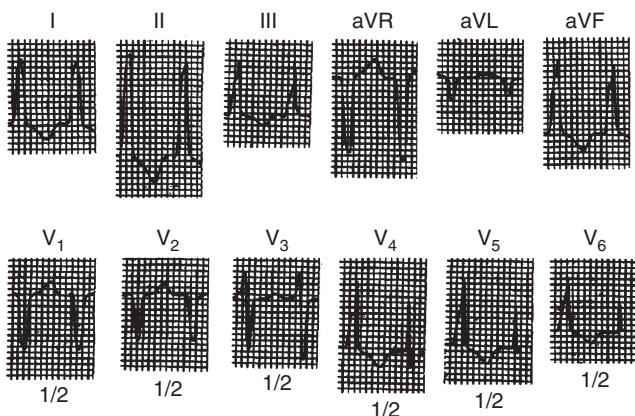
1. Most of the tools suggested for the investigation of PVCs are used for VT, including (1) ECGs (for QTc prolongation or ST-T changes), (2) echo studies (for cardiomyopathy and other structural and functional abnormalities), (3) 24-hour Holter monitoring or event recorder, and (4) exercise stress testing (for induction or exacerbation or elimination of arrhythmia with exercise). MRI is useful to rule out arrhythmogenic RV dysplasia. Electrophysiologic studies and possible ablation, and endomyocardial biopsy are required for some patients.
2. Acute therapy may include the following.
 - a. Prompt synchronized cardioversion (0.5 to 1.0 joules/kg) if the patient is unconscious or if there is evidence of low cardiac output.
 - b. If the patient is conscious, an IV bolus of lidocaine, 1 mg/kg over 1 to 2 min, followed by an IV drip of lidocaine, 20 to 50 $\mu\text{g/kg/min}$, may be effective.
3. Intravenous amiodarone is used in patients with drug-refractory VT, particularly that seen in postoperative patients.
4. Patients with long QT syndrome are treated with β -blockers, which alleviate symptoms in 75% to 80%. An implantable cardioverter-defibrillator (ICD) is sometimes recommended as initial therapy.
5. Recurrence may be prevented with administration of propranolol, atenolol, diphenylhydantoin, or quinidine. A combination of 24-hour Holter monitoring and treadmill exercise testing is the best noninvasive means of evaluating drug effectiveness.
6. Some incessant ventricular tachycardias are amenable to radiofrequency ablation.
7. ICD has become the established standard for treating many, if not most, forms of ventricular tachycardia, which are potentially lethal.

Ventricular Arrhythmias in Children with Normal Hearts

Although recurrent sustained VT usually signals an organic cause of the arrhythmia, some VTs are seen in healthy adolescents and young adults with structurally and functionally normal hearts. The prognosis is good. Right ventricular outflow tract VT and RBBB VT are examples of this group of VT.

Right Ventricular Outflow Tract (RVOT) Ventricular Tachycardia

1. **Description:** This special form of VT originates from the RV conal septum and thus has inferior QRS axis and LBBB morphology (see [Fig. 16-7](#)). This is usually benign tachycardia. It may manifest as frequent PVCs or short runs or salvos of VT but many children are asymptomatic or

**FIGURE 16-7**

Tracing from a 4-year-old asymptomatic girl with RVOT ventricular tachycardia. The rate of ventricular tachycardia was 160 beats/min. The QRS complexes have LBBB morphology indicating the RV as the ectopic focus and the axis of VT is directed inferiorly. Spontaneous temporary interruption of VT occurred while recording V4, V5, and V6 leads. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.).

minimally symptomatic. Exercise stress may not completely abolish the tachycardia.

2. **Treatment:** β -blockers are sufficient for treatment. Verapamil and other agents may also prove to be effective. Radiofrequency ablation can be curative.

RBBB Ventricular Tachycardia (Belhassen Tachycardia)

1. **Description:** It appears to arise from the septal surface of the LV and is less common than RVOT VT. It is characterized by RBBB morphology and superior QRS axis.
2. **Treatment:** They may be calcium channel dependent and respond to slow IV push of verapamil. Long-term treatment with verapamil can prevent recurrences. When refractory to medical therapy, radiofrequency ablation or surgery is effective. The long-term outcome is excellent.

Ventricular Fibrillation

1. **Description:** Ventricular fibrillation is characterized by bizarre QRS complexes of varying sizes and configurations. The rate is rapid and irregular (see Fig 16-6).
2. **Causes:** Postoperative state, severe hypoxia, hyperkalemia, digitalis or quinidine toxicity, myocarditis, myocardial infarction, and drugs (catecholamines, anesthetics, etc.) are possible causes.
3. **Significance:** It is usually fatal because it results in ineffective circulation.

4. **Treatment:** Immediate cardiopulmonary resuscitation, including electric defibrillation at 2 joules/kg, is required. Implantable cardioverter defibrillators (ICDs) are often indicated in patients who survived ventricular fibrillation.

Long QT Syndrome

Description

Long QT syndrome (LQTS) is a genetic disorder of ventricular repolarization characterized by a prolonged QT interval on the ECG and ventricular arrhythmias, usually torsades de pointes that may result in sudden death.

Causes

1. Congenital types: Ion channels that govern the electrical activity of the heart are defective in congenital LQTS.
 - a. Jervell and Lange-Nielsen syndrome (autosomal recessive mode) consists of a prolonged QTc interval, congenital deafness, syncopal spells, and a family history of sudden death.
 - b. Roman-Ward syndrome (autosomal dominant mode) has all the features of Jervell and Lange-Nielsen syndrome except for deafness. A sporadic form of the syndrome with a negative family history also exists.
 - c. In Anderson-Tawil syndrome, the QU interval (rather than QT interval) is prolonged, along with muscle weakness (periodic paralysis), ventricular arrhythmias, and developmental abnormalities.
 - d. Timothy syndrome is associated with webbed fingers and toes and a prolonged QTc interval.
2. Acquired type. Prolongation of the QT interval can be caused by a number of drugs, electrolyte disturbances, and other underlying medical conditions ([Box 16-1](#)). A similar ionic mechanism may be involved as in congenital LQTS. Those individuals who manifest acquired long QT syndrome are believed to be genetically predisposed for the condition.

Clinical Manifestations

1. Positive family history is present in about 60% and deafness in 5% of patients.
2. Presenting symptoms may be syncope (26%), seizure (10%), cardiac arrest (9%), presyncope, or palpitation (6%).
3. Symptoms usually occur in the setting of intense adrenergic arousal, intense emotion, and during or following rigorous exercise. Swimming appears to be a particular trigger. A loud doorbell, alarm clock, telephone, or security alarm can trigger symptoms.
4. The ECG shows the following:
 - a. The QTc interval is prolonged, usually to >0.46 second. The upper limit of normal QTc is 0.44 second.
 - b. Abnormal T wave morphology (bifid, diphasic, or notched) is frequent.
 - c. Bradycardia (20%), second-degree AV block, multiform PVCs, and monomorphic or polymorphic VT may be present.

5. Echo studies usually show a structurally and functionally normal heart.
6. A treadmill exercise test results in a highly significant prolongation of the QTc interval, with the maximal QTc prolongation present after 1 to 2 minutes of recovery. Ventricular arrhythmias may develop during the test in up to 30% of patients.
7. Holter monitoring reveals prolongation of the QTc interval, major changes in the T wave configuration (T wave alternation), and ventricular arrhythmias. The QTc interval on Holter monitor may be longer than that recorded on a standard ECG (see a later section).

Diagnosis

A correct diagnosis and proper treatment can save lives, but the diagnosis of this disease should not be made lightly, because it implies a high-risk disease with a lifelong commitment to treatment.

1. Accurate measurement of the QTc interval is essential in the diagnosis of long QT syndrome.
 - a. Lead II (with q waves) and precordial leads (V1, V3, or V5, with well-defined T waves) are good leads in measuring the QT interval.
 - b. In patients with sinus arrhythmia, the QT interval immediately following the shortest RR interval has been recommended to use in calculating the QTc interval. However, the QTc measurement during sinus arrhythmia may not be reliable because Bazett formula is reliable only for the steady state and sinus arrhythmia is not a steady state.
 - c. In patients with wide QRS complexes (such as BBB), the JTc interval may be a more sensitive predictor of repolarization abnormalities than the QTc. Rate correction is accomplished by the use of Bazett formula. Normal JTc interval (mean \pm SD) is 0.32 ± 0.02 second (with the upper limit of normal 0.34 second).
2. Schwartz diagnostic criteria. The diagnosis of long QT syndrome is clear-cut when there is a marked prolongation of the QTc interval with positive family history of the syndrome. However, many cases are borderline, making it difficult to make or reject the diagnosis. Schwartz et al refined diagnostic criteria using a point system (Table 16-1) as follows.
 - a. ≤ 1 point = low probability of LQTS
 - b. 2 to 3 points = intermediate probability of LQTS
 - c. ≥ 4 points = high probability LQTS
3. Initial diagnostic strategy: The following steps are considered in making the diagnosis of LQTS.
 - a. History of presyncope, syncope, seizure, or palpitation and family history are carefully examined.
 - b. Causes of acquired LQTS are excluded.
 - c. The ECG is examined for the QTc interval and morphology of the T waves. ECGs are also obtained from immediate family members.
 - d. The LQTS score is calculated (see Table 16-1) and the diagnostic possibility is graded as described previously.
 - (1) Patients with an LQTS score ≥ 4 are considered to have LQTS.

TABLE 16-1
SCHWARTZ DIAGNOSTIC CRITERIA FOR LONG QT SYNDROME

ECG FINDINGS (in the absence of medications or disorders known to prolong the QTc interval)	
QTc	
>480 msec	3
460–470 msec	2
450 (male) msec	1
<i>Torsades de pointes</i>	2
T-wave alternans	1
Notched T waves in three leads	1
Low heart rate for age (<2nd percentile)	0.5
CLINICAL HISTORY	
Syncope with stress	2
Syncope without stress	1
Congenital deafness	0.5
FAMILY HISTORY	
Family members with definite LQTS	1
Unexplained sudden cardiac death <30 yr among immediate family members	0.5

Adapted from Schwartz PJ, Moss AJ, Vincent GM, Crampton RS: Diagnostic criteria for the long QT syndrome: an update. *Circulation* 88:782–784, 1993.

- (2) Those with an LQTS score ≤ 1 are excluded from the diagnosis.
- (3) Those with an LQTS score of 2 or 3 are followed up for possible LQTS.
- e. For borderline cases, some centers carry out additional testing, such as Holter monitoring, exercise testing, pharmacologic testing, or electrophysiology study. However, the interpretation and significance of these tests are controversial.
- 4. Genetic testing may identify genotypes of the LQTS. The commercially available genetic tests can identify the five most common gene mutations, all in Romano Ward syndrome (including KCNQ1, KCNE1, KCNH2, KCNE2, and SCN5A). The genetic testing has limitations, though. It is important to realize that the testing can identify a particular mutation but it cannot rule out LQTS; a negative genetic test does not rule out LQTS.

Management

- 1. The following are known risk factors for sudden death and they should be considered when making a treatment plan.
 - a. Bradycardia for age (sinus bradycardia, junctional escape rhythm, or second-degree AV block).
 - b. An extremely long QTc interval (>0.55 second).
 - c. Symptoms at presentation (syncope, seizure, cardiac arrest).
 - d. Young age at presentation (< 1 month).
 - e. Documented torsades de pointes or ventricular fibrillation.
 - f. T wave alternans (major changes in T wave morphology) is a relative risk factor.

2. General measures
 - a. Physicians should avoid prescribing medications that prolong the QT interval, including some commonly used antibiotics and catecholamines. See [Box 16-1](#) and check on updated Internet sources such as www.torsades.org or www.qtdrugs.org.
 - b. No competitive sports are allowed. Swimming is not advised.
 - c. Alarm clocks or bedside telephones should be removed because these are known triggers of VT in patients with LQTS.
 - d. The patients and the parents should be educated about the importance of being compliant with their medication, because noncompliance can result in sudden death.
3. Treatment of congenital LQTS
 - a. β -blockers. β -blockers are the current treatment of choice. They reduce both syncope and sudden cardiac death but cardiac events continue to occur while on β -blocker therapy.
 - (1) There is a consensus that all symptomatic children with long QT syndrome should be treated with propranolol, atenolol, or metoprolol.
 - (2) Whether to start β -blockers on asymptomatic children with QTc prolongation is controversial.
 - (a) Any patients who score 4 or greater on the Schwartz diagnostic criteria should be treated regardless of symptoms.
 - (b) It may be prudent to follow those asymptomatic children with borderline QTc intervals (0.46 to 0.47). Symptoms are more likely to occur in patients with QTc intervals >0.48 seconds. In addition, β -blockers may be dangerous, because they tend to produce bradycardia, a known risk factor for sudden death.
 - (3) Schwartz (1997) has recommended definite treatment in the following circumstances: (a) newborns and infants, (b) patients with deafness, (c) affected siblings with LQTS and sudden cardiac death, (d) extremely long QTc (>0.60 sec) or T wave alternans, and (e) to prevent family or patient anxiety.
 - b. The ICD appears to be the most effective therapy for high-risk patients, defined as those with aborted cardiac arrests or recurrent cardiac events despite conventional therapy (with β -blockers), and those with extremely prolonged QTc intervals (e.g., >0.60 second). Patients with ICD should be kept on β -blockers.
 - c. Left cardiac sympathetic denervation. Because of the availability of other options, such as ICD, this procedure is rarely performed.
 - d. Targeted pharmacologic therapy. The sodium channel blocker mexiletine was used in patients with mutation in the sodium channel gene *SCN5A* (*LQT3*) with significant shortening of the QTc. Gene or gene-specific therapy has not gained wide clinical application at this time.

Prognosis

The prognosis is very poor in untreated patients, with annual mortality as high as 20% and 10-year mortality of 50%. β -blockers may reduce

mortality to some extent, but they do not completely protect patients from sudden death. The ICD appears promising in improving prognosis.

Short QT Syndrome

1. **Description:** Short QT syndrome is characterized by a very short QTc (≤ 300 millisecond), symptoms of palpitation, dizziness or syncope, and family history of sudden death. The cause of death is believed to be ventricular fibrillation. This syndrome is transmitted in an autosomal dominant manner. Although the death usually occurs in the adult (median age 30 years), a sudden cardiac death was observed in infancy.
2. **Treatment:** Recently, the use of an antiarrhythmic agent, particularly quinidine (which prolongs the QT interval) has been suggested. An ICD may become standard practice.

Brugada Syndrome

Description

This inherited arrhythmogenic disorder with a high risk of sudden cardiac death from ventricular tachyarrhythmia, occurring during sleep, appears to be inherited as an autosomal dominant pattern. It is primarily a disease of adult males, seen most commonly in Southeast Asian men (with mean age of 40 years). However, this syndrome has been demonstrated in children and infants. No male preponderance is observed in children, raising the possibility of a high level of androgen in the occurrence of the fatal event. Mutations in the sodium channel (*SCN5A*) appear to be the cause of the condition, at least in 20% of the patients.

Clinical Manifestations

1. Cardiac examination is usually normal. There is no demonstrable structural abnormality of the heart.
2. The ECG typically shows concave ST segment elevation (> 2 mm) with J point elevation followed by a negative T wave in the right precordial leads (V1-V3) and RBBB appearance. This so-called type-1 ECG pattern may be present either spontaneously or after provocation with ajmaline or flecainide. The PR interval is frequently prolonged.
3. Most syncope takes place at rest (90%).
4. Diagnosis is suspected based on the ECG appearance, which may not always be present.

Treatment

1. β -blockers do not appear to reduce the risk of death in these patients.
2. In many centers, ICD is standard practice to prevent sudden cardiac death.
3. Hydroquinidine has been shown to be a good alternative to ICD implantation in adult patients and it appears to be effective in preventing syncope in children also.

Atrioventricular Conduction Disturbances

Atrioventricular (AV) block is a disturbance in conduction between the normal sinus impulse and the eventual ventricular response. The block is assigned to one of three classes, according to the severity of the conduction disturbance.

1. First-degree AV block is a simple prolongation of the PR interval but all P waves are conducted to the ventricle.
2. In second-degree AV block, some atrial impulses are not conducted into the ventricle.
3. In third-degree AV block (or complete heart block), none of the atrial impulses is conducted into the ventricle (Fig. 17-1).

I. FIRST-DEGREE AV BLOCK

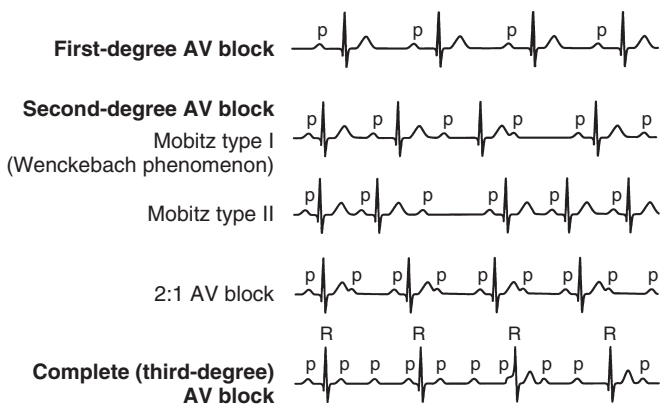
1. **Description:** There is a prolongation of the PR interval beyond the upper limits of normal (see Table 2-3) due to an abnormal delay in conduction through the AV node (see Fig. 17-1).
2. **Causes**
 - a. In otherwise healthy children and young adults, particularly athletes, mediated through excessive parasympathetic tone.
 - b. CHDs (such as endocardial cushion defect, ASD, Ebstein anomaly).
 - c. Other causes including infectious disease, inflammatory conditions (rheumatic fever), cardiac surgery, and certain drugs (such as digitalis, calcium channel blockers).
3. **Significance**
 - a. Usually no hemodynamic disturbance results. Exercise, both recreational and during stress testing, induces parasympathetic withdrawal resulting in normalization of AV conduction and the PR interval.
 - b. Sometimes it may progress to a more advanced AV block.
4. **Treatment:** No treatment is indicated except in digitalis toxicity.

II. SECOND-DEGREE AV BLOCK

In second-degree AV block, some but not all P waves are followed by QRS complexes (dropped beats). There are three types: Mobitz type I (Wenckebach phenomenon), Mobitz type II, and high-grade (or advanced) second-degree AV block.

A. Mobits Type I (Wenckebach Phenomenon)

1. **Description:** The PR interval becomes progressively prolonged until one QRS complex is dropped completely (see Fig. 17-1).

**FIGURE 17-1**

Atrioventricular (AV) block. (From Park MK, Guntheroth WG: *How to Read Pediatric ECGs*, ed 4, Philadelphia, Mosby, 2006.)

- Causes:** In otherwise healthy children, myocarditis, cardiomyopathy, myocardial infarction, CHD, cardiac surgery, and digitalis toxicity.
- Significance**
 - The block is at the level of the AV node (with prolonged AH interval).
 - It occurs in individuals with vagal dominance.
 - It usually does not progress to complete heart block.
- Treatment:** The underlying cause is treated.

B. Mobitz Type II

- Description:** The AV conduction is “all or none.” AV conduction is either normal or completely blocked (see Fig. 17-1).
- Causes:** Same as for Mobitz type I.
- Significance:**
 - The block usually occurs below the AV node (at the level of the bundle of His).
 - It is more serious than type I block, because it may progress to complete heart block, resulting in Stokes-Adams attacks.
- Treatment:** The underlying cause is treated. Prophylactic pacemaker therapy may be indicated.

C. Two-to-One (or Higher) AV Block

Description

- A QRS complex follows every second (third or fourth) P wave, resulting in 2:1 (3:1 or 4:1, respectively) AV block (see Fig. 17-1). In contrast to third-degree complete AV block, some P waves continue to be conducted to the ventricle and the PR interval of conducted beats is constant.

2. When two or more consecutive P waves are nonconducted, the rhythm is called advanced or high-grade second-degree AV block.

Causes

Similar to those of other second-degree AV blocks.

Significance

1. The block is usually at the bundle of His, alone or in combination with the AV nodal block.
2. It may occasionally progress to complete heart block.
3. Higher-grade second-degree AV block should always be regarded as abnormal. The implications of high-grade AV block appear to be similar to those of complete AV block.

Treatment

The underlying cause is treated. Electrophysiologic studies may be necessary to determine the level of the block. Pacemaker therapy is indicated for symptomatic advanced second-degree AV block.

III. THIRD-DEGREE AV BLOCK (COMPLETE HEART BLOCK)

Description

1. In third-degree AV block, the atrial and ventricular activities are entirely independent of each other (see Fig. 17-1). The P waves are regular (with regular PP interval) with a rate comparable to the heart rate of the patient's age. The QRS complexes are also quite regular (with regular RR interval) but with a rate much slower than the P rate.
2. The third-degree AV block is either congenital or acquired.
 - a. In *congenital* complete heart block, the duration of the QRS complex is normal, since the pacemaker for the QRS complex is at a level higher than the bifurcation of the bundle of His. The ventricular rate is faster (50 to 80 beats/min) than in the acquired type.
 - b. In surgically induced or *acquired* (from postmyocardial infarction) complete heart block, the QRS duration is prolonged, and the ventricular rate is in the range of 40 to 50 beats/min (idioventricular rhythm). The pacemaker for the wide QRS complex is at a level below the bifurcation of the bundle of His.

Causes

1. Congenital heart block
 - a. In 60% to 90% of cases, it is caused by neonatal lupus erythematosus. Maternal antibodies for autoimmune connective tissue diseases cross the placenta to the fetus causing the heart block.
 - b. In 25% to 33%, it is associated with CHDs, most commonly with L-TGA, single ventricle, or polysplenia syndrome.
 - c. Neonatal myocarditis and several genetic disorders such as familial ASD and Kearns-Sayre syndrome have been identified.

2. The acquired type
 - a. It occurs as a complication of cardiac surgery in children.
 - b. Rarely, severe myocarditis, Lyme carditis, acute rheumatic fever, mumps, diphtheria, cardiomyopathies, tumors in the conduction system, or overdose of certain drugs causes the block.
 - c. It may also follow myocardial infarction.
 - d. These causes produce either temporary or permanent heart block.

Significance

1. Complete heart block can be diagnosed by fetal bradycardia during fetal echo study between 18 and 28 weeks of gestation. Complications *in utero* may include hydrops fetalis, myocarditis, and fetal death.
2. CHF may develop in infancy, particularly when there are associated CHDs.
3. Patients with isolated congenital heart block are usually asymptomatic during childhood and achieve normal growth and development.
4. Syncopal attacks (Stokes-Adams attack) or sudden death may occur with the heart rate below 40 to 45 beats/min.

Treatment

1. Atropine or isoproterenol is indicated in symptomatic children and adults until temporary ventricular pacing is secured.
2. Asymptomatic children with congenital complete heart block with acceptable heart rate, narrow QRS complex, and normal ventricular function may not need to be treated.
3. Pacemaker therapy is indicated in patients with congenital heart block under the following situations (see Box 18-1 for detailed indications).
 - a. If the patient is symptomatic or develops CHF.
 - b. Dizziness or lightheadedness may be an early warning sign of the need for a pacemaker.
 - c. If an infant has a ventricular rate <50 to 55 beats/min or if the infant has a CHD with a ventricular rate <70 beats/min.
 - d. If the patient has a wide QRS escape rhythm, complex ventricular ectopy or ventricular dysfunction.
4. A permanent artificial ventricular pacemaker is indicated in patients with surgically induced heart block that is not expected to resolve or that persists at least 7 days after cardiac surgery.

A. Atrioventricular Dissociation

Atrioventricular (AV) dissociation should not be confused with complete heart block (third-degree AV block).

1. AV dissociation results from a marked slowing of the sinus node activity, atrial bradycardia, or acceleration of the AV node.

**FIGURE 17-2**

Diagram of AV dissociation owing to either marked slowing of the sinus node or acceleration of the AV node. The fourth complex is conducted, changing the rhythm (called “interference”).

2. In AV dissociation the atrial rate is slower than the ventricular rate, whereas in complete heart block the ventricular rate is usually slower than the atrial rate.
3. In AV dissociation an atrial impulse may conduct to the AV node if it comes at the right time (Fig. 17-2). The conducted beat can be recognized by its relative prematurity.

Chapter 18

Pacemakers and Implantable Cardioverter Defibrillators

I. PACEMAKERS IN CHILDREN

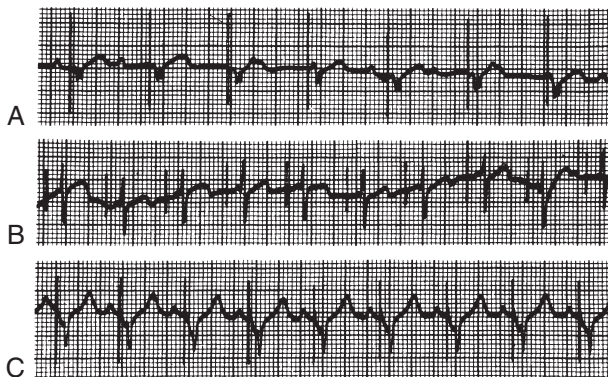
A pacemaker is a device that delivers battery-supplied electrical stimuli over leads to electrodes in contact with the heart. The electrical leads are inserted either directly over the epicardium or transvenously; the latter is the method of choice. Electronic circuitry regulates the timing and characteristics of the stimuli. The power source usually is a lithium-iodine battery. Battery life varies from 3 years to 15 years depending on the type of the device, which determines the amount of battery use. New pacemakers are capable of closely mimicking normal cardiac rhythm (physiologic pacemakers), and most of them are small enough to be implanted in an infant.

Physicians encounter an increasing number of children with either temporary or permanent pacemakers. Basic knowledge about the pacemaker and the pacemaker rhythm strip is essential in taking care of these children.

A. ECGs of Artificial Cardiac Pacemakers

1. **Rhythm strips of artificial pacemakers:** The need to recognize rhythm strips of artificial pacemakers has increased in recent years, especially in intensive care and emergency room settings. The position and number of the pacemaker spikes on the ECG rhythm strip are used to recognize different types of pacemakers.
 - a. When the pacemaker stimulates the atrium, a P wave follows an electronic spike. The resulting P wave demonstrates an abnormal P axis.
 - b. When the pacemaker stimulates the ventricle, a wide QRS complex appears after the electronic spike.
 - c. The ventricle that is stimulated (or the ventricle on which the pacemaker electrode is placed) can be identified by the morphology of the QRS complexes. With the pacing electrode on the RV, the QRS complex resembles an LBBB pattern; with the pacemaker placed on the LV, an RBBB pattern results.
2. **Examples of pacemaker ECGs:** Three examples of pacemaker ECGs are shown in [Figure 18-1](#).
 - a. Ventricular pacemaker (ventricular sensing and pacing). This mode of pacing is recognized by vertical pacemaker spikes that initiate ventricular depolarization with wide QRS complexes ([Fig. 18-1, A](#)). The electronic spike has no fixed relationship with atrial activity (P

- wave). The pacemaker rate may be fixed as in the figure, or it may be on a demand (or standby) mode in which the pacemaker fires only after a long pause between the patient's own ventricular beats.
- b. Atrial pacemaker (atrial sensing and pacing). The atrial pacemaker is recognized by a pacemaker spike followed by an atrial complex. When atrioventricular (AV) conduction is normal, a QRS complex of normal duration follows (see Fig. 18-1, B). This type of pacemaker is indicated in patients with sinus node dysfunction with bradycardia. When the patient has high-degree or complete AV block in addition to sinus node dysfunction, an additional ventricular pacemaker may be required (AV sequential pacemaker, not illustrated in the figure). The AV sequential pacemaker is recognized by two sets of electronic spikes, one before the P wave and another before the wide QRS complex.
 - c. P-wave triggered ventricular pacemaker (atrial sensing, ventricular pacing). This type of pacemaker can be recognized by pacemaker spikes that follow the patient's own P waves at regular PR intervals and with wide QRS complexes (see Fig. 18-1, C). The patient's own P waves are sensed and trigger a ventricular pacemaker after an electronically preset PR interval. This type of pacemaker is the most physiologic and is indicated when the patient has advanced AV block but a normal sinus mechanism. Advantages of this type of pacemaker are that the heart rate varies with physiologic need and the atrial contraction contributes to ventricular filling and improves cardiac output.

**FIGURE 18-1**

Examples of some artificial pacemaker rhythm strips. **A**, Fixed-rate ventricular pacemaker. **B**, Atrial pacemaker. **C**, P wave-triggered pacemaker. Note that tall spikes in **A** and **C** are electronic spikes, not the QRS complexes.

B. Indications

Box 18-1 lists conditions for which pacemaker therapy is or is not indicated, based on the 2008 joint recommendations of the American College of Cardiology (ACC), American Heart Association (AHA), and Heart Rhythm Society (HRS).

1. In general, the most common indications for permanent pacemaker implantation in children, adolescents, and patients with CHD fit into one of three categories:
 - a. Symptomatic bradycardia (with symptoms of syncope, dizziness, exercise intolerance, or congestive heart failure). In children, significant bradycardia with syncope or near syncope results most commonly from extensive surgery involving the atria (such as the Fontan operation).

BOX 18-1**RECOMMENDATIONS FOR PERMANENT PACING IN CHILDREN, ADOLESCENTS, AND PATIENTS WITH CONGENITAL HEART DISEASE****CLASS I (IS INDICATED)**

1. For advanced second- or third-degree associated with symptomatic bradycardia, ventricular dysfunction, or low cardiac output. (*Level of Evidence: C*)
2. For sinus node dysfunction with correlation of symptoms during age-inappropriate bradycardia. The definition of bradycardia varies with the patient's age and expected heart rate. (*Level of Evidence: B*)
3. For postoperative advanced second- or third-degree AV block that is not expected to resolve or that persists at least 7 days after cardiac surgery. (*Level of Evidence: B*)
4. For congenital third-degree AV block with a wide QRS escape rhythm, complex ventricular ectopy, or ventricular dysfunction. (*Level of Evidence: B*)
5. For congenital third-degree AV block in the infant with a ventricular rate less than 55 bpm or with congenital heart disease and a ventricular rate less than 70 bpm. (*Level of Evidence: C*)

CLASS IIA (IS REASONABLE)

1. For patients with congenital heart disease and sinus bradycardia for the prevention of recurrent episodes of intraatrial re-entrant tachycardia; sinus node dysfunction may be intrinsic or secondary to antiarrhythmic treatment. (*Level of Evidence: C*)
2. For congenital third-degree AV block beyond the first year of life with an average heart rate less than 50 bpm, abrupt pauses in ventricular rate that are 2 or 3 times the basic cycle length, or associated with symptoms due to chronotropic incompetence. (*Level of Evidence: B*)
3. For sinus bradycardia with complex congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 seconds. (*Level of Evidence: C*)
4. For patients with congenital heart disease and impaired hemodynamics due to sinus bradycardia or loss of AV synchrony. (*Level of Evidence: C*)
5. For unexplained syncope in the patient with prior congenital heart surgery complicated by transient complete heart block with residual fascicular block after a careful evaluation to exclude other causes of syncope. (*Level of Evidence: B*)

BOX 18-1
RECOMMENDATIONS FOR PERMANENT PACING IN CHILDREN, ADOLESCENTS, AND PATIENTS WITH CONGENITAL HEART DISEASE (Continued)
CLASS IIB (MAY OR MIGHT BE REASONABLE)
<div>1. For transient postoperative third-degree AV block that reverts to sinus rhythm with residual bifascicular block. (<i>Level of Evidence: C</i>)</div> <div>2. For congenital third-degree AV block in asymptomatic children or adolescents with an acceptable rate, a narrow QRS complex, and normal ventricular function. (<i>Level of Evidence: B</i>)</div> <div>3. For asymptomatic sinus bradycardia after biventricular repair of congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 seconds. (<i>Level of Evidence: C</i>)</div>
CLASS III (IS NOT INDICATED)
<div>1. For transient postoperative AV block with return of normal AV conduction in the otherwise asymptomatic patient. (<i>Level of Evidence: B</i>)</div> <div>2. For asymptomatic bifascicular block with or without first-degree AV block after surgery for congenital heart disease in the absence of prior transient complete AV block. (<i>Level of Evidence: C</i>)</div> <div>3. For asymptomatic type I second-degree AV block. (<i>Level of Evidence: C</i>)</div> <div>4. For asymptomatic sinus bradycardia with the longest relative risk interval less than 3 seconds and a minimum heart rate more than 40 bpm. (<i>Level of Evidence: C</i>)</div>

Adapted from Epstein AE, DiMarco JP, Ellenbogen KA, et al: ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices), *Circulation* 117:2820-2840, 2008.

- b. The bradycardia-tachycardia syndrome (due to overdrive suppression after a period of tachycardia).

c. Advanced second- or third-degree AV block, either congenital or postsurgical.
2. Another noncontroversial indication is surgically acquired heart block that lasts more than 7 days after surgery.
3. Temporary pacing is indicated for (1) patients with advanced second-degree or complete heart block secondary to overdose of certain drugs, myocarditis, or myocardial infarction and (2) certain patients immediately after cardiac surgery.

C. Types of Pacing Devices

The North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and Electrophysiology Group (BPEG) devised a generic letter code to describe the types and functions of pacemakers (Table 18-1).

1. The letter in the first position identifies the chamber paced (A, atrium; V, ventricle; D, dual) and the second is the chamber sensed (A, atrium; V, ventricle; D, dual; O, none). The third letter corresponds to the

TABLE 18-1
REVISED NASPE/BPEG GENERIC CODE FOR ANTIBRADYCARDIA PACING

I: CHAMBER(S) PACED	II: CHAMBER(S) SENSED	III: RESPONSE TO SENSING	IV: PROGRAMMABILITY, RATE MODULATION	V: ANTIARRHYTHMIA FUNCTION
O, None	O, None	O, None	O, None	O, None
A, Atrium	A, Atrium	T, Triggered	R, Rate modulation	A, Atrium
V, Ventricle	V, Ventricle	I, Inhibited		V, Ventricle
D, Dual (A + V)	D, Dual (A + V)	D, Dual (T + I)		D, Dual (A + V)

NASPE, North American Society of Pacing and Electrophysiology; BPEG, British Pacing and Electrophysiology Group.
Adapted from Bernstein AD, Daubert AC, Fletcher RD, et al, and The NASPE/BPEG: The revised NASPE/BPEG generic code for antibradycardia, adaptive-rate, and multisite pacing, *Pacing Clin Electrophysiol* 25:260-264, 2002.

response of the pacemaker to an intrinsic cardiac event (I, inhibited; T, triggered; D, dual). For example:

- a. A VOO device provides ventricular pacing, no sensing, and no response. This type of pacemaker is commonly used for emergency pacing.
 - b. A VVI device is ventricle stimulated and ventricle sensed; it inhibits paced output if endogenous ventricular activity occurs (thus preventing competition with native QRS activity). This type is commonly used for episodic AV block or bradycardia in small infants.
 - c. An AAI device paces and senses the atrium and is inhibited by atrial activity. This type is commonly used in patients with sinus node dysfunction with intact AV conduction.
 - d. A DDD device is a dual-chamber pacemaker that is capable of pacing either chamber, sensing activity in either chamber, and either triggering or inhibiting paced output (with resulting AV synchrony). This type is used in AV block where AV synchrony is important.
2. The pacemaker choice is based on several factors, including the presence or absence of underlying cardiac disease, the size of the patient, and the relevant hemodynamic factors (including the need for atrial contribution in cardiac output).

II. IMPLANTABLE CARIOVERTER DEFIBRILLATOR

A. Description

- 1. An implantable cardioverter defibrillator (ICD) is used in patients at risk for recurrent, sustained ventricular tachycardia or fibrillation. The efficacy of ICD therapy in saving lives of patients at high risk of sudden death has been shown convincingly.
- 2. All ICDs also have a built-in pacemaker. The ICD automatically detects, recognizes, and treats tachyarrhythmias and bradyarrhythmias using tiered therapy (i.e., bradycardia pacing, overdrive tachycardia pacing, low-energy cardioversion, high-energy shock defibrillation). ICDs can discharge voltages ranging from less than 1 V for pacing to 750 V for defibrillation.
- 3. The ICD is implanted beneath the skin over the left chest (for right-handed persons) pectoralis muscle and the leads are connected to the ICD. Virtually all ICD systems are implanted transvenously.

4. The longevity of the ICD depends on the frequency of shock delivery, the degree of pacemaker dependency, and other programmable options, but most are expected to last from 5 to 10 years.
5. The most common problem with the ICD is inappropriate shocks, which are usually the result of detection of a supraventricular tachycardia, most commonly atrial fibrillation. In adult patients, inappropriate shock has been reported in up to 20% of patients within the first year and 40% by 2 years after implantation, causing pain and anxiety generated by this complication.

B. Indications

Box 18-2 lists recommendations for ICD therapy according to the 2008 ACC/AHA/HRS Guidelines.

1. The two most common indications for ICD implantation in children are hypertrophic cardiomyopathy and long QT syndrome.
2. Other potential indications include idiopathic dilated cardiomyopathy, Brugada syndrome, and arrhythmogenic RV dysplasia.
3. A family history of sudden death may influence the decision to use an ICD in a pediatric patient.
4. Some postoperative CHDs with ventricular tachycardia, such as TOF and TGA, are rare indications for ICD implantation.

III. LIVING WITH A PACEMAKER OR ICD

Electromagnetic interference (EMI) can cause malfunction of the pacemaker or ICD by rate alteration, sensing abnormalities, reprogramming, and other functions, which may result in malfunction of the device or even damage to the pulse generator. Patients should be educated to avoid situations that may cause malfunction or damages to the device. EMI can occur within or outside the hospital. Patients with pacemakers should wear medical identification bracelets or necklaces in case of emergency to show that they have the pacemaker or ICD.

A. Potential Sources of Electromagnetic Interference

The following are some common situations that may or may not affect pacemakers or ICDs.

1. Most home appliances in the following list will NOT interfere with the pacemaker signal.
 - a. Kitchen appliances (microwave ovens, blenders, toaster ovens, electric knives)
 - b. Televisions, stereos, FM and AM radios, ham radios, CB radios
 - c. Electric blankets, heating pads
 - d. Electric shavers, hair dryers, curling irons
 - e. Garage door openers, gardening electric trimmers
 - f. Computers, copying and fax machines
 - g. Properly grounded shop tools (except power generator or arc welding equipment)

BOX 18-2**RECOMMENDATIONS FOR IMPLANTABLE CARDIOVERTER DEFIBRILLATORS
IN PEDIATRIC PATIENTS AND PATIENTS WITH CONGENITAL HEART DISEASE****CLASS I (IS INDICATED)**

1. In the survivors of cardiac arrest after evaluation to define the cause of the event and to exclude any reversible causes. (*Level of Evidence: B*)
2. For patients with symptomatic sustained VT in association with congenital heart disease who have undergone hemodynamic and electrophysiologic evaluation. Catheter ablation or surgical repair may offer possible alternatives in carefully selected patients. (*Level of Evidence: C*)

CLASS IIA (IS REASONABLE)

1. For patients with congenital heart disease with recurrent syncope of undetermined origin in the presence of either ventricular dysfunction or inducible ventricular arrhythmias at electrophysiologic study. (*Level of Evidence: B*)

CLASS IIB (MAY OR MIGHT BE REASONABLE)

1. For patients with recurrent syncope associated with complex congenital heart disease and advanced systemic ventricular dysfunction when thorough invasive and noninvasive investigations have failed to define a cause. (*Level of Evidence: C*)

CLASS III (IS NOT INDICATED). THE SAME AS IN ADULTS.

1. For patients who do not have a reasonable expectation of survival with an acceptable functional status for at least 1 year, even if they meet ICD implantation criteria specifics in Class I, Ila, and I Ib recommendations. (*Level of Evidence: C*)
2. For patients with incessant VT or VF. (*Level of Evidence: C*)
3. In patients with significant psychiatric illness that may be aggravated by device implantation or that may preclude systematic follow-up. (*Level of Evidence: C*)
4. For NYHA Class IV patients with drug-refractory congestive heart failure who are not candidates for cardiac transplantation or CTR-D. (*Level of Evidence: C*)
5. For syncope of undetermined cause in a patient without inducible ventricular tachycardias and without structural heart disease. (*Level of Evidence: C*)
6. When VF or VT is amenable to surgical or catheter ablation (e.g., atrial arrhythmias associated with the Wolff-Parkinson-White syndrome, RV or LV outflow tract VT, idiopathic VT, or fascicular VT in the absence of structural heart disease. (*Level of Evidence: C*)
7. For patients with ventricular tachyarrhythmias due to a completely reversible disorder in the absence of structural heart disease (e.g., electrolyte imbalance, drugs, or trauma). (*Level of Evidence: B*)

Adapted from Epstein AE, DiMarco JP, Ellenbogen KA, et al: ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices), *Circulation* 117:2820–2840, 2008.

CRT-D, cardiac resynchronization therapy device incorporating both pacing and defibrillation capabilities; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia.

2. The patient must use caution in the following situations.
 - a. Security detectors at airport and government buildings such as court-houses. The patient should not stay near the electronic article surveillance system longer than is necessary and should not lean against the system.
 - b. Cellular phones; the patient should not carry a cell phone in the breast pocket when the ICD is implanted in the left upper chest. Keep the cell phone at least 6 inches away from the ICD. When talking on the cell phone, hold it on the opposite side of the body from the ICD.
 - c. Avoid working with, holding, or carrying magnets near the pacemaker.
 - d. Turn off large motors, such as cars or boats, when working on them. Do not use a chain saw.
 - e. Avoid industrial welding equipment. Most welding equipment used for “hobby” welding should not cause any significant problem.
 - f. Avoid high-tension wires, radar installations, smelting furnaces, electric steel furnaces, and other high-current industrial equipment.
 - g. Abstain from diathermy (the use of heat to treat muscles).
 - h. Contact sports are not recommended for children with a pacemaker or ICD.
3. Hospital sources of potentially significant EMI are as follows.
 - a. Electrocautery during surgical procedures. Notify surgeon or dentist so that electrocautery will not be used to control bleeding. ICD therapy should be deactivated before surgery and reinitiated after surgery by a qualified professional. Alternatively, a magnet can be placed over the pacemaker throughout the procedure.
 - b. For cardioversion or defibrillation. Paddles should be placed in the anteroposterior position, keeping the paddles at least 4 inches from the pulse generator. A qualified pacemaker programmer should be available.
 - c. Magnetic resonance imaging (MRI) is considered a relative contraindication in patients with a pacemaker or ICD.

B. Follow-Up for Pacemaker and ICD

1. Patients with pacemakers and ICDs must be followed on a regular schedule because a variety of problems may arise after a pacemaker is placed in children. Problems may arise from stress placed on the lead system by the linear growth of the child, fracture of the lead system in a physically active child, electrode malfunction (scarring of the myocardium around the electrode, especially in infants), and the limited life span of the pulse generator. Many of the same considerations are relevant to both pacemaker and ICD follow-up.
2. Some physicians prefer regular office assessment, others prefer transtelephonic follow-up, and still others prefer a combination of the two techniques. The frequency of clinic follow-up and pacemaker interrogation by the pacemaker manufacturer varies between 3 and 12 months. Monthly transtelephonic evaluation is simple, convenient, and inexpensive.

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SPECIAL PROBLEMS

This part explores common pediatric cardiac problems not discussed in previous chapters. The topics include (1) congestive heart failure, (2) child with chest pain, (3) syncope, (4) palpitation, (5) systemic hypertension, (6) pulmonary hypertension, (7) athletes with cardiac problems, and (8) lipid abnormalities (dyslipidemia).

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Congestive Heart Failure

Congestive heart failure (CHF) is a clinical syndrome in which the heart is unable to pump enough blood to the body to meet its needs, to dispose of systemic or pulmonary venous return adequately, or a combination of the two.

A. Causes

The heart failure syndrome may arise from diverse causes. By far the most common causes of CHF in infancy are CHDs. Beyond infancy, myocardial dysfunction of various etiologies is an important cause of CHF. Tachyarrhythmias and heart block can also cause heart failure at any age.

1. Congenital heart disease

- a. Volume overload lesions such as VSD, PDA, and ECD are the most common causes of CHF in the first 6 months of life.
- b. In infancy, the time of the onset of CHF varies predictably with the type of defect. [Table 19-1](#) lists common defects according to the age at which CHF develops.
- c. Large L-R shunt lesions, such as VSD and PDA, do not cause CHF before 6 to 8 weeks of age because the pulmonary vascular resistance (PVR) does not fall low enough to cause a large shunt until this age. CHF may occur earlier in premature infants (within the first month) because of an earlier fall in the PVR.
- d. Note that children with TOF do not develop CHF and that ASDs rarely cause CHF in the pediatric age group, although they can cause CHF in adulthood.

2. Acquired heart disease. Acquired heart disease of various etiologies can lead to CHF. Common entities (with the approximate time of onset of CHF) are as follows.

- a. Viral myocarditis (in toddlers, occasionally in neonates with fulminating course).
- b. Myocarditis associated with Kawasaki disease (1 to 4 years of age).
- c. Acute rheumatic carditis (in school-age children).
- d. Rheumatic valvular heart diseases, such as MR or AR (older children and adults).
- e. Dilated cardiomyopathy (at any age during childhood and adolescence).
- f. Doxorubicin cardiomyopathy (months to years after chemotherapy).
- g. Cardiomyopathies associated with muscular dystrophy and Friedrich's ataxia (in older children and adolescents).

3. Miscellaneous causes

- a. Metabolic abnormalities (severe hypoxia, acidosis, hypoglycemia, hypocalcemia) (in newborns)

TABLE 19-1
CAUSES OF CONGESTIVE HEART FAILURE RESULTING FROM CONGENITAL HEART DISEASE

AGE OF ONSET	CAUSE
At birth	HLHS
	Volume overload lesions
	Severe tricuspid or pulmonary insufficiency
First wk	Large systemic arteriovenous fistula
	TGA
	PDA in small premature infants
	HLHS (with more favorable anatomy)
	TAPVR with pulmonary venous obstruction
	Critical AS or PS
1-4 wk	Systemic arteriovenous fistula
	COA with associated anomalies
	Critical AS
	Large left-to-right shunt lesions (VSD, PDA) in premature infants
	All other lesions previously listed
4-6 wk	Some left-to-right shunt lesions such as ECD
6 wk-4 mo	Large VSD
	Large PDA
	Others such as anomalous left coronary artery from the PA

AS, aortic stenosis; COA, coarctation of the aorta; ECD, endocardial cushion defect; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery; PDA, patent ductus arteriosus; PS, pulmonary stenosis; TAPVR, total anomalous pulmonary venous return; TGA, transposition of the great arteries; VSD, ventricular septal defect.

- b. Hyperthyroidism (at any age)
- c. Supraventricular tachycardia (SVT) (in early infancy)
- d. Complete heart block associated with CHDs (in the newborn period or early infancy)
- e. Severe anemia (at any age), hydrops fetalis (neonates), and sick-
lemlia (childhood and adolescence)
- f. Bronchopulmonary dysplasia (BPD) with right-sided failure (the first
few months of life)
- g. Primary carnitine deficiency (2-4 years)
- h. Acute cor pulmonary caused by acute airway obstruction (during
early childhood)
- i. Acute systemic hypertension with glomerulonephritis (school-age
children)

B. Diagnosis of CHF

The diagnosis of CHF relies on several sources of clinical findings, including history, physical examination, chest radiographs, and echo studies. There is no single laboratory test that is diagnostic of CHF in pediatric patients.

- 1. Poor feeding of recent onset, tachypnea, poor weight gain, and cold
sweat on the forehead suggest CHF in infants. In older children,

shortness of breath, especially with activities, easy fatigability, puffy eyelids, or swollen feet may be presenting complaints.

2. Physical findings can be divided by pathophysiologic subgroups.
 - a. Compensatory responses to impaired cardiac function.
 - (1) Tachycardia, gallop rhythm, weak and thready pulse, and cardiomegaly on chest radiographs.
 - (2) Signs of increased sympathetic discharges (growth failure, perspiration, and cold wet skin).
 - b. Signs of pulmonary venous congestion (left-sided failure) include tachypnea, dyspnea on exertion (or poor feeding in small infants), orthopnea in older children, and rarely wheezing and pulmonary crackles.
 - c. Signs of systemic venous congestion (right-sided failure) include hepatomegaly and puffy eyelids. Distended neck veins and ankle edema are not seen in infants.
3. Cardiomegaly on chest radiograph is almost always present, except when the pulmonary venous return is obstructed; in that case pulmonary edema or venous congestion will be present.
4. The ECG is not helpful in deciding whether the patient is in CHF, although it may be helpful in determining the cause.
5. Echo studies confirm the presence of chamber enlargement or impaired LV function and help determine the cause of CHF.
6. Increased levels of plasma natriuretic peptides (atrial natriuretic peptide [ANP] and B-type natriuretic peptide [BNP]) are helpful in differentiating causes of dyspnea (lungs vs. heart) in adult patients, but the usefulness of the levels of these peptides is limited in pediatric use. Plasma levels of these peptides are normally elevated in the first weeks of life.
7. Endomyocardial biopsy obtained during cardiac catheterization offers a new approach to specific diagnosis of the cause of CHF, such as inflammatory disease, infectious process, or metabolic disorder.

C. Management

The treatment of CHF consists of (1) elimination of the underlying causes or correction of precipitating or contributing causes (e.g., infection, anemia, arrhythmias, fever, hypertension), (2) general supportive measures, and (3) control of heart failure state by use of drugs, such as inotropic agents, diuretics, or afterload-reducing agents.

1. Treatment of underlying causes or contributing factors.
 - a. Treatment or surgery of underlying CHDs or valvular heart disease when feasible (the best approach for complete cure).
 - b. Antihypertensive treatment for hypertension.
 - c. Antiarrhythmic agents or cardiac pacemaker therapy for arrhythmias or heart block.
 - d. Treatment of hyperthyroidism if it is the cause of CHF.
 - e. Antipyretics for fever.
 - f. Antibiotics for a concomitant infection.
 - g. Packed cell transfusion for anemia (to raise the hematocrit to $\geq 35\%$).

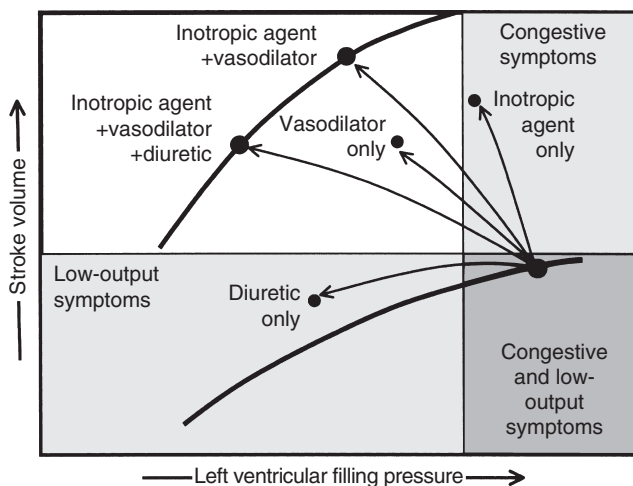
BOX 19-1

INCREASING CALORIC DENSITY OF FEEDINGS

1. Human milk fortifier (Enfamil, Mead Johnson), 1 packet per 25 ml of breast milk = 24 kcal/oz
2. Formula concentration to 24 kcal/oz by:
 - a. 1 cup powdered formula + 3 cups water or
 - b. 4 oz ready-to-feed + ½ scoop powdered formula
3. Supplementation of formula to 26-30 kcal/oz is accomplished in the following manner.
 - a. Fat modular products
 - (1) Medium chain triglycerides (MCT) oil (Mead Johnson), 8 kcal/mL
 - (2) Microlipid (safflower oil emulsion, Mead Johnson), 4.5 kcal/mL
 - b. Low-osmolality polymers
 - (1) Polycose (Ross), 23 kcal/teaspoon
 - (2) Moducal (Mead Johnson), 30 kcal/teaspoon
4. Pediasure (Ross), 30 kcal/oz ready-to-feed (for children over 1 year of age)

From Wright GE, Rochini AP: Primary and general care of the child with congenital heart disease, ACC Current Journal Review, Mar/Apr: 89-93, 2002.

2. General measures.
 - a. Nutritional supports are important. Infants in CHF need significantly higher caloric intakes than recommended for average children. The required calorie intakes may be as high as 150 to 160 kcal/kg/day for infants in CHF.
 - b. Increasing caloric density of feeding may be required and it may be accomplished with fortification of feeding (see [Box 19-1](#)). Frequent small feedings are better tolerated than large feedings in infants.
 - c. If oral feedings are not well tolerated, intermittent or continuous nasogastric (NG) feeding is indicated. To promote normal development of oral-motor function, infants may be allowed to take calorie-dense oral feeds throughout the day and then be given continuous NG feeds overnight.
 - d. For older children with heart failure, salt restriction (<0.5 g/day) and avoidance of salty snacks (chips, pretzels) and table salt are recommended. Bed rest remains an important component of management. The availability of a television and computer games for entertainment assures bed rest in older children.
3. **Drug therapy.** Three major classes of drugs are commonly used in the treatment of CHF in children: inotropic agents, diuretics, and afterload-reducing agents.
 - a. **Effects of drugs on the Frank-Starling relationship.** Effects of anticongestive medications on the Frank-Starling relationship for ventricular function are illustrated in [Figure 19-1](#). In persons with normal hearts, cardiac output increases as a function of ventricular filling pressure (preload) (see the upper curve in [Fig. 19-1](#)). In patients with heart failure (the lower curve), the normal relationship between cardiac outputs (stroke volume) and filling pressure (preload) is shifted

**FIGURE 19-1**

Effects of anticongestive medications on the Frank-Starling relationship for ventricular function. See text for explanation. (Adapted from Cohn JN, Franciosa JS. Vasodilator therapy of cardiac failure [first of two parts], *N Engl J Med* 297:27-31, 1977).

downward and to the right so that a low-output state and congestive symptoms may coexist. If the filling pressure reaches a certain point, congestive symptoms (dyspnea, tachypnea) may appear even in a normal heart (shown in the right side of the rectangle in Fig. 19-1).

- (1) The addition of a pure inotropic agent, such as digoxin, in patients with congestive symptoms will not relieve the symptoms. Inotropic agents primarily increase the stroke volume with minimal impact on filling pressure (see “Inotropic agent only” in Fig. 19-1).
- (2) The addition of a diuretic primarily decreases the filling pressure (with improved congestive symptoms) but without improving cardiac output (see “Diuretic only” in Fig. 19-1).
- (3) Clinically, it is common to use multiple classes of agents (usually a combination of inotropic agents, diuretics, and vasodilators) to produce both increased cardiac output and decreased filling pressure.

b. Diuretics.

- (1) Diuretics remain the principal therapeutic agent to control pulmonary and systemic venous congestion. Diuretics only reduce preload and improve congestive symptoms, but do not improve cardiac output or myocardial contractility (see Fig. 19-1). Three classes of diuretics are available.
 - (a) Thiazide diuretics (e.g., chlorothiazide, hydrochlorothiazide), which act at the proximal and distal tubules, are no longer popular.

TABLE 19-2		
DIURETIC AGENTS AND DOSAGES		
PREPARATION	ROUTE	DOSAGE
THIAZIDE DIURETICS		
Chlorothiazide (Diuril)	Oral	20-40 mg/kg/day in 2 to 3 divided doses
Hydrochlorothiazide (HydroDIURIL)	Oral	2-4 mg/kg/day in 2 to 3 divided doses
LOOP DIURETICS		
Furosemide (Lasix)	IV	1 mg/kg/dose
	Oral	2-3 mg/kg/day in 2 to 3 divided doses
Ethacrynic acid (Edecrin)	IV	1 mg/kg/dose
	Oral	2-3 mg/kg/day in 2 to 3 divided doses
ALDOSTERONE ANTAGONIST		
Spironolactone (Aldactone)	Oral	1-3 mg/kg/day in 2 to 3 divided doses

- (b) Rapid-acting diuretics (e.g., furosemide, ethacrynic acid) are the drugs of choice. They act primarily at the loop of Henle (“loop diuretics”).
 - (c) Aldosterone antagonist (e.g., spironolactone) acts on the distal tubule to inhibit sodium-potassium exchange. These drugs have value in preventing hypokalemia produced by other diuretics and thus are used in conjunction with a loop diuretic. However, when ACE inhibitors are used, spironolactone should be discontinued to avoid hyperkalemia.
- (2) The main side effects of diuretic therapy are hypokalemia (except when used with spironolactone) and hypochloremic alkalosis.
- (3) [Table 19-2](#) shows dosages of commonly available diuretic preparations.
- c. **Rapidly acting inotropic agents.**
- (1) In critically ill infants with CHF, rapidly acting catecholamines with a short duration of action are preferable to digoxin. Suggested dosages of this class of inotropic agent are shown in [Table 19-3](#).
 - (2) Amrinone is a noncatecholamine agent that exerts its inotropic effect and vasodilator effects by inhibiting phosphodiesterase (see Appendix E for dosage). Thrombocytopenia is a side effect; the drug should be discontinued if the platelet count falls below 150,000/mm³.
- d. **Digitalis glycosides.**
- (1) Digoxin increases the cardiac output (or contractile state of the myocardium), thereby resulting in an upward and leftward shift of the ventricular function curve relating cardiac output to filling volume of pressure (see [Fig. 19-1](#)). Use of digoxin in infants with large L-R shunt lesions (e.g., large VSD) is controversial because ventricular contractility is normal in this situation. However, studies have shown that digoxin improves symptoms in these infants, perhaps because of other actions of digoxin, such as parasympathomimetic action and diuretic action.

TABLE 19-3**SUGGESTED STARTING DOSAGES OF CATECHOLAMINES**

DRUG	DOSAGE AND ROUTE	SIDE EFFECTS
Epinephrine (Adrenalin)	0.1-1 µg/kg/min IV	Hypertension, arrhythmias
Isoproterenol (Isuprel)	0.1-0.5 µg/kg/min IV	Peripheral and pulmonary vasodilatation
Dobutamine (Dobutrex)	2-8 µg/kg/min IV	Little tachycardia and vasodilatation, arrhythmias
Dopamine (Intropin)	5-10 µg/kg/min IV	Tachycardia, arrhythmias, hypertension or hypotension Dose-related cardiovascular effects (µg/kg/min): Renal vasodilatation: 2-5 Inotropic: 5-8 Tachycardia: >8 Mild vasoconstriction: >10 Vasoconstriction: 15-20

TABLE 19-4**ORAL DIGOXIN DOSAGE FOR CONGESTIVE HEART FAILURE**

AGE	TOTAL DIGITALIZING DOSE (µg/kg)	MAINTENANCE DOSE* (µg/kg/day)
Premature	20	5
Newborns	30	8
<2 yr	40-50	10-12
>2 yr	30-40	8-10

*The maintenance dose is 25% of the total digitalizing dose in two divided doses. The IV dose is 75% of the oral dose.

Adapted from Park MK: The use of digoxin in infants and children with specific emphasis on dosage, *J Pediatr* 108:871-877, 1986.

- (2) **Dosage of digoxin.** The total digitalizing dose (TDD) and maintenance dosage of digoxin by oral and intravenous routes are shown in Table 19-4. The maintenance dose is more closely related to the serum digoxin level than is the digitalizing dose, which is given to build a sufficient body store of the drug and to shorten the time required to reach the pharmacokinetic steady state.
- (3) **How to digitalize.**
- One half the total digitalizing dose is followed by one fourth and then the final one fourth of the total digitalizing dose at 6- to 8-hour intervals. The maintenance dose is given 12 hours after the final total digitalizing dose. This results in a pharmacokinetic steady state in 3 to 5 days.
 - When an infant is in mild heart failure, the maintenance dose may be administered orally without loading doses; this results in a steady state in 5 to 8 days.
 - A baseline ECG (rhythm and PR interval) and serum electrolytes are recommended. Hypokalemia and hypercalcemia predispose to digitalis toxicity.

(4) **Monitoring for digitalis toxicity.**

- (a) With the relatively low dosage recommended in [Table 19-4](#), digitalis toxicity is unlikely unless there are predisposing factors for the toxicity. Predisposing factors for digitalis toxicity may include renal disease, premature infants, hypothyroidism, myocarditis, electrolyte imbalance (hypokalemia and hypercalcemia), alkalosis, and catecholamine administration.
- (b) Serum digoxin levels obtained during the first 3 to 5 days after digitalization tend to be higher than those obtained when the pharmacokinetic steady state is reached. Therefore, detection of digitalis toxicity is best accomplished by monitoring with ECGs, not by serum digoxin levels during this period.
- (c) ECG signs of digitalis toxicity involve disturbances in the formation and conduction of the impulse, while those of digitalis effect are confined to ventricular repolarization. First-degree (or second-degree) AV block, profound sinus bradycardia or sinoatrial block, supraventricular arrhythmias (atrial or junctional ectopic beats and tachycardias), and, rarely, ventricular arrhythmias are all possible signs of toxicity. Shortening of QTc and diminished amplitude of the T wave are the signs of digitalis effect.

(5) **Serum digoxin levels.** Therapeutic ranges of serum digoxin levels for treating CHF are 0.8 to 2 ng/mL. Blood for serum digoxin levels should be drawn just before a scheduled dose or at least 6 hours after the last dose; samples obtained earlier than 6 hours after the last dose will give a falsely elevated level.

(6) **Digitalis toxicity.** The diagnosis of digitalis toxicity is based on the following clinical and laboratory findings.

- (a) A history of accidental ingestion.
- (b) Noncardiac symptoms in digitalized children: anorexia, nausea, vomiting, diarrhea, restlessness, drowsiness, fatigue, and visual disturbances in older children.
- (c) ECG signs of toxicity (as described previously).
- (d) An elevated serum level of digoxin (>2 mg/mL) in the presence of clinical findings suggestive of digitalis toxicity.

e. **Afterload-reducing agents.**

(1) Reducing afterload tends to augment the stroke volume without a great change in the inotropic state of the heart and therefore without increasing myocardial oxygen consumption. Combined use of an inotropic agent, a vasodilator, and a diuretic produces most improvement in both inotropic state and congestive symptoms ([Fig. 19-1](#)).

(2) Afterload-reducing agents may be used not only in infants with a large-shunt VSD, AV canal, or PDA, but also in patients with dilated cardiomyopathies, myocardial ischemia, postoperative cardiac status, severe MR or AR, and systemic hypertension. Dosages of the afterload-reducing agents are presented in [Table 19-5](#).

TABLE 19-5

DOSAGES OF VASODILATORS

DRUG	ROUTE AND DOSAGE	COMMENTS
ARTERIORLAR VASODILATOR		
Hydralazine (Apresoline)	IV: 0.15–0.2 mg/kg/dose, every 4 to 6 hr (maximum 20 mg/dose) Oral: 0.75–3 mg/kg/day, in 2 to 4 doses (maximum 200 mg/day)	May cause tachycardia; may be used with propranolol May cause gastrointestinal symptoms, neutropenia, and lupus-like syndrome
VENODILATORS		
Nitroglycerin	IV: 0.5–1 μ g/kg/min (maximum 6 μ g/kg/min)	Start with small dose and titrate based on effects
MIXED VASODILATORS		
Captopril (Capoten)	Oral: Newborn: 0.1–0.4 mg/kg, TID–QID Infant: Initially 0.15–0.3 mg/kg, QD–QID. Titrate upward if needed. Max dose 6 mg/kg/24 hr. Child: Initially 0.3–0.5 mg/kg, BID–TID. Titrate upward if needed. Max dose 6 mg/kg/24 hr. Adolescents and adults: Initially 12.5–25 mg, BID–TID. Increase weekly if needed by 25 mg/dose to max dose 450 mg/24 hr.	May cause hypotension, dizziness, neutropenia, and proteinuria Dose should be reduced in patients with impaired renal function
Enalapril (Vasotec)	Oral: 0.1 mg/kg, once or twice daily	Patient may develop hypotension, dizziness, or syncope
Nitroprusside (Nipride)	IV: 0.3–0.5 μ g/kg/min. Titrate to effects. (Max dose 10 μ g/kg/min)	May cause thiocyanate or cyanide toxicity (e.g., fatigue, nausea, disorientation), hepatic dysfunction, or light sensitivity

f. Other drugs.

(1) β -Adrenergic blockers

- As reported in adults, β -adrenergic blockers have been shown to be beneficial in some pediatric patients with chronic CHF, who were treated with standard anticongestive drugs. Adrenergic overstimulation, often seen in patients with chronic CHF, may have detrimental effects on the failing heart by inducing myocyte injury and necrosis. However, β -adrenergic blockers should not be given to those with decompensated heart failure.
- When added to standard medical therapy for CHF, carvedilol (a nonselective β -adrenergic blocker with additional α_1 -antagonist activities) has been shown to be beneficial in children with idiopathic dilated cardiomyopathy,

chemotherapy-induced cardiomyopathy, postmyocarditis myopathy, muscular dystrophy, or postsurgical heart failure (e.g., Fontan operation).

- (c) Metoprolol was also beneficial in dilated cardiomyopathy.
- (d) Propranolol added to conventional treatment for CHF was also beneficial in a small number of infants with large L-R shunts at the dose of 1.6 mg/kg per day.

- (2) **Carnitine.** Carnitine, which is an essential cofactor for transport of long-chain fatty acids into mitochondria for oxidation, has been shown to be beneficial in some cases of dilated cardiomyopathy. The dosage of L-carnitine used was 50-100 mg/kg/day, given BID or TID orally (maximum daily dose 3 g).

- 4. **Surgical management.** If medical treatment as outlined previously does not improve CHF caused by CHD within a few weeks to months, one should consider either palliative or corrective cardiac surgery for the underlying cardiac defect when technically feasible.

Child with Chest Pain

Although chest pain does not indicate serious disease of the heart or other systems in most pediatric patients, in a society with a high prevalence of atherosclerotic heart disease, it can be alarming to the child and parents. Physicians should be aware of the differential diagnosis of chest pain in children and should make every effort to find a specific cause before making a referral to a specialist or reassuring the child and the parents of the benign nature of the complaint.

I. CAUSE AND PREVALENCE

1. Cardiac causes of chest pain are found in less than 5% of children with complaint of chest pain. Noncardiac causes of chest pain are found in 56% to 86% of reported cases.
2. [Table 20-1](#) lists the frequency of the causes of chest pain in children according to organ systems based on published data from six pediatric emergency departments and four pediatric cardiology clinics. According to the table, the three most common causes of chest pain in children are (1) costochondritis, (2) chest wall trauma or muscle strain, and (3) respiratory diseases, especially those associated with coughing.
3. Gastrointestinal and psychogenic causes are identified in fewer than 10% of cases.
4. Even after a moderately extensive investigation, no cause can be found in up to 50% of patients (idiopathic chest pain).
5. In children with chronic chest pain, a cardiac cause is less likely to be found.
6. [Box 20-1](#) is a partial list of *possible* causes of noncardiac and cardiac chest pain in children.

A. Noncardiac Causes of Chest Pain

1. **Costochondritis**
 - a. Costochondritis is found in up to 80% of children with chest pain. It is more common in girls than boys and may persist for several months. It is characterized by mild to moderate anterior chest pain, usually unilateral but occasionally bilateral. The pain may radiate to the remainder of the chest and back, and may be exaggerated by breathing or physical activities. Physical examination is diagnostic; the clinician finds a reproducible tenderness on palpation over the chondrosternal or costochondral junctions. It is a benign condition.
 - b. *Tietze syndrome* is a rare form of costochondritis characterized by a large, tender fusiform (spindle-shaped), nonsuppurative swelling

TABLE 20-1
FREQUENCY OF CAUSES OF CHEST PAIN IN CHILDREN

CAUSES	PEDIATRIC EMERGENCY DEPARTMENT OR PEDIATRIC CLINIC (DATA FROM 6 REPORTS) (%)	CARDIOLOGY CLINIC (DATA FROM 4 REPORTS) (%)
Idiopathic/cause unknown	12-61	37-54
Musculoskeletal/costochondritis	7-69	1-89
Respiratory/asthma	13-24	1-12
Gastrointestinal/gastroesophageal reflux disease	3-7	3-12
Psychogenic	5-9	4-19
Cardiac	2-5	3-7

From Thull-Freedman J: Evaluation of chest pain in the pediatric patients, Med Clin N Am 94:327-347, 2010.

BOX 20-1
SELECTED CAUSES OF CHEST PAIN

NONCARDIAC CAUSES

Musculoskeletal

- Costochondritis
- Trauma to chest wall (from sports, fights, or accident)
- Muscle strains (pectoral, shoulder, or back muscles)
- Overused chest wall muscle (from coughing)
- Abnormalities of the rib cage or thoracic spine
- Tietze syndrome
- Slipping rib syndrome
- Precordial catch (Texidor's twinge or stitch in the side)

Respiratory

- Reactive airway disease (exercise-induced asthma)
- Pneumonia (viral, bacterial, mycobacterium, fungal, or parasitic)
- Pleural irritation (pleural effusion)
- Pneumothorax or pneumomediastinum
- Pleurodynia (devil's grip)
- Pulmonary embolism
- Foreign bodies in the airway

Gastrointestinal

- Gastroesophageal reflux
- Peptic ulcer disease
- Esophagitis
- Gastritis
- Esophageal diverticulum
- Hiatal hernia
- Foreign bodies (such as coins)
- Cholecystitis
- Pancreatitis

Psychogenic

- Life stressor (death in family, family discord, divorce, failure in school, nonacceptance from peers, or sexual molestation)
- Hyperventilation

BOX 20-1**SELECTED CAUSES OF CHEST PAIN (Continued)****Psychogenic (Continued)**

- Conversion symptoms
- Somatization disorder
- Depression
- Bulimia nervosa (esophagitis, esophageal tear)

Miscellaneous

- Sickle cell disease (vaso-occlusive crisis)
- Mastalgia
- Herpes zoster

CARDIAC CAUSES**Ischemic Ventricular Dysfunction**

- Structural abnormalities of the heart (severe AS or PS, hypertrophic obstructive cardiomyopathy, Eisenmenger syndrome)
- Mitral valve prolapse
- Coronary artery abnormalities (previous Kawasaki disease, congenital anomaly, coronary heart disease, hypertension, sickle cell disease)
- Cocaine abuse
- Aortic dissection and aortic aneurysm (Turner, Marfan, or Noonan syndromes)

Inflammatory Conditions

- Pericarditis (viral, bacterial, or rheumatic)
- Postpericardiectomy syndrome
- Myocarditis (acute or chronic)
- Kawasaki disease

Arrhythmias (and Palpitations)

- Supraventricular tachycardia
- Frequent PVCs or ventricular tachycardia (possible)

at the chondrosternal junction. It usually affects the second and third costochondral junctions.

2. **Musculoskeletal.** There is a history of vigorous exercise, weight lifting, or direct trauma to the chest. Physical examination reveals tenderness of the chest wall or pectoralis muscles.
3. **Respiratory.** Lung pathology, pleural irritation, or pneumothorax account for 10% to 20% of the cases. A history of severe cough, tenderness of intercostal or abdominal muscles, and crackles or wheezing on examination suggest a respiratory cause of chest pain.
4. **Exercise-induced asthma.** Exercise-induced asthma is not that uncommon. The response of the asthmatic patient to exercise is quite characteristic. The intensity of exercise is important. Strenuous exercise for 3 to 8 minutes' duration causes bronchoconstriction in virtually all asthmatic subjects, especially when the heart rate rises to 180 beats per minute. On the other hand, jogging or slow running for 1 to 2 minutes often causes bronchodilatation. Symptoms range from mild to severe and may include coughing, wheezing, dyspnea, and chest congestion, constriction, or pain. Patients also complain of limited endurance during

exercise. Environmental factors such as cold temperature, pollen, and air pollution, as well as viral respiratory infection can worsen exercise-induced asthma. Exercise-induced bronchospasm provocation test is diagnostic (discussed under Stress Tests in Chapter 5).

5. **Gastrointestinal**

- a. Gastroesophageal reflux disease (GERD) may cause chest pain. In addition to chest pain, children with GERD may complain of abdominal pain, frequent sore throat, gagging or choking, frequent respiratory problems (such as bronchitis, wheezing, asthma), and poor weight gain. The onset and relief of pain in relation to eating and diet may help clarify the diagnosis.
- b. In young children, ingested foreign bodies (such as coins or caustic substances) may cause chest pain.
- c. Cholecystitis presents with postprandial pain referred to the right upper quadrant of the abdomen and part of the chest.

6. **Psychogenic.** Psychogenic causes are less likely to be found in children younger than 12 years old, and are more likely to be found in females older than 12 year of age. Often a recent stressful situation parallels the onset of the chest pain: a death or separation in the family, a serious illness, a disability, a recent move, failure in school, or sexual molestation. However, a psychological cause of chest pain should not be lightly assigned without a thorough history taking and a follow-up evaluation. Psychological or psychiatric consultation may be indicated.

7. **Miscellaneous**

- a. The precordial catch (Texidor's twinge or stitch in the side), a one-sided chest pain, lasts a few seconds or minutes and is associated with bending or slouching.
- b. Slipping rib syndrome (resulting from excess mobility of the eighth to tenth ribs, which do not directly insert into the sternum). In many cases the ligaments that hold these ribs to the upper ribs are weak, resulting in slippage of the ribs, causing pain.
- c. Mastalgia in some male and female adolescents.
- d. Pleurodynia (devil's grip) is an unusual cause of chest pain caused by coxsackievirus infection.
- e. Herpes zoster is another unusual cause of chest pain.
- f. Spontaneous pneumothorax and pneumomediastinum are rare respiratory causes of acute chest pain. Children with asthma, cystic fibrosis, or Marfan syndrome are at risk. Inhalation of cocaine can provoke pneumomediastinum and pneumothorax.
- g. Hyperventilation can produce chest discomfort and is often associated with paresthesia and lightheadedness.

B. Cardiac Causes of Chest Pain

Cardiac chest pain may be caused by ischemic ventricular dysfunction, pericardial or myocardial inflammatory processes, or arrhythmias, occurring in less than 5% of cases (**Box 20-1**). **Table 20-2** summarizes important clinical findings of cardiac causes of chest pain in children.

TABLE 20-2

IMPORTANT CLINICAL FINDINGS OF CARDIAC CAUSES OF CHEST PAIN

CONDITIONS	HISTORY	PHYSICAL FINDINGS	ECG	CHEST RADIOGRAPHY
Severe AS	Hx of CHD (+)	Loud (> grade 3/6 SEM at URSB with radiation to neck)	LVH with or without strain	Prominent ascending aorta and aortic knob
Severe PS	Hx of CHD (+)	Loud (grade >3/6) SEM at ULSB	RVH with or without strain	Prominent PA segment
HOCM	Positive FH in one third of cases	Variable heart murmurs Brisk brachial pulses (\pm)	LVH Deep Q/small R or QS pattern in LPLs	Mild cardiomegaly with globular-shaped heart
MVP	Positive FH (\pm)	Midsystolic click with or without late systolic murmur Thin body build Thoracic skeletal anomalies (80%)	Inverted T waves in aVF (\pm)	Normal heart size Straight back (\pm) Narrow anteroposterior diameter (\pm)
Eisenmenger syndrome	Hx of CHD (+)	Cyanosis and clubbing RV impulse Loud and single S2 Soft or no heart murmur	RVH	Markedly prominent PA with normal heart size
Anomalous origin of left coronary artery	Recurrent episodes of distress in early infancy	Soft or no heart murmur	Anterolateral MI pattern	Moderate to marked cardiomegaly
Sequelae of Kawasaki or other coronary artery diseases	Hx of Kawasaki disease (\pm) Typical exercise-related anginal pain	Usually negative Continuous murmur in coronary fistula	ST-segment elevation (\pm) Old MI pattern (\pm)	Normal heart size or mild cardiomegaly
Cocaine abuse	Hx of substance abuse (\pm)	Hypertension Nonspecific heart murmur (\pm)	ST-segment elevation (\pm)	Normal heart size in acute cases

Continued

TABLE 20-2

IMPORTANT CLINICAL FINDINGS OF CARDIAC CAUSES OF CHEST PAIN (Continued)

CONDITIONS	HISTORY	PHYSICAL FINDINGS	ECG	CHEST RADIOGRAPHY
Pericarditis and myocarditis	Hx of URI (±) Sharp chest pain	Friction rub Muffled heart sounds Nonspecific heart murmur (±)	Low QRS voltages ST-segment shift Arrhythmias (±)	Cardiomegaly of varying degree
Postpericardiotomy syndrome	Hx of recent heart surgery, pain, and dyspnea	Muffled heart sounds (±) Friction rub	Persistent ST-segment elevation	Cardiomegaly of varying degree
Arrhythmias (and palpitation)	Hx of WPW syndrome (±) FH of long QT syndrome (±)	May be negative Irregular rhythm (±)	Arrhythmias (±) WPW preexcitation (±) Long QTc interval (>0.46 sec)	Normal heart size

AS, aortic stenosis; CHD, congenital heart disease; FH, family history; HOCM, hypertrophic obstructive cardiomyopathy; Hx, history; LPLs, left precordial leads; LVH, left ventricular hypertrophy; MI, myocardial infarction; MVP, mitral valve prolapse; PA, pulmonary artery; PS, pulmonary stenosis; RV, right ventricle; RVH, right ventricular hypertrophy; SEM, systolic ejection murmur; ULSB, upper left sternal border; URI, upper respiratory infection; URSB, upper right sternal border; WPW, Wolff-Parkinson-White; (+), positive; (±), may be present.

1. Ischemic myocardial dysfunction
 - a. Congenital heart defects. Severe AS, subaortic stenosis, severe PS, and pulmonary hypertension (Eisenmenger syndrome) may cause ischemic chest pain. The pain is usually associated with exercise and is a typical anginal pain.
 - b. Mitral valve prolapse. Chest pain associated with MVP is usually a vague, nonexertional pain of short duration, located at the apex, without a constant relationship to effort or emotion. Occasionally, supraventricular or ventricular arrhythmias may result in cardiac symptoms, including chest discomfort. Nearly all patients with Marfan syndrome have MVP. A midsystolic click with or without a late systolic murmur is the hallmark of the condition.
 - c. Cardiomyopathy. Hypertrophic and dilated cardiomyopathies can cause chest pain from ischemia, with or without exercise, or from rhythm disturbances.
 - d. Coronary artery disease. Coronary artery anomalies, either congenital (aberrant or single coronary artery, coronary artery fistula) or acquired (aneurysm or stenosis of the coronary arteries as a result of Kawasaki disease or as a result of previous cardiac surgery involving the coronary arteries) can rarely cause chest pain.
 - e. Cocaine abuse. Even children with normal hearts are at risk of ischemia and myocardial infarction if cocaine is used. Cocaine blocks the reuptake of norepinephrine with an increase in circulating levels of catecholamines causing coronary vasoconstriction. Cocaine also induces the activation of platelets, increases endothelin production, and decreases nitric oxide production. These effects collectively produce anginal pain, infarction, arrhythmias, or sudden death. History and drug screening help physicians in the diagnosis of cocaine-induced chest pain.
2. Pericardial or myocardial disease
 - a. Pericarditis. Older children with pericarditis may complain of a sharp, stabbing precordial pain that worsens when lying down and improves after sitting and leaning forward. Echo examination is usually diagnostic.
 - b. Myocarditis. Acute myocarditis often involves the pericardium to a certain extent and can cause chest pain.
3. Arrhythmias. Chest pain may result from a variety of arrhythmias, especially with sustained tachycardia resulting in myocardial ischemia. Even without ischemia, children may consider palpitation or forceful heartbeats as chest pain. In this situation, chest pain may be associated with dizziness and palpitation.

II. DIAGNOSTIC APPROACH

Careful history and physical examination usually suffice in detecting the three common noncardiac causes of chest pain and in ruling out cardiac causes of the pain in most children with chest pain. Occasionally additional studies may be needed depending on history and physical findings to rule out cardiac causes.

1. History of present illness

History taking should ask about the nature of the pain, in terms of its association with exertion or physical activities, the intensity, character, frequency, duration, and points of radiation. The following are some examples of questions used in determining the nature of chest pain.

- a. What seems to bring on the pain (e.g., exercise, eating, trauma, emotional stress)?
- b. Do you get the same type of pain while you watch TV or sit in class?
- c. What is the pain like (e.g., sharp, pressure sensation, squeezing)?
- d. What are the location (e.g., specific point, localized or diffuse), severity, radiation, and duration (seconds, minutes) of the pain?
- e. Does the pain get worse with deep breathing? (If so, the pain may be caused by pleural irritation or chest wall pathology.) Does the pain improve with certain body positions? (This is sometimes seen with pericarditis.)
- f. Does the pain have any relationship with your meals?
- g. How often and how long have you had similar pain (frequency and chronicity)?
- h. Have you been hurt while playing, or have you used your arms excessively for any reason?
 - i. Are there any associated symptoms, such as presyncope, syncope, dizziness, or palpitation?
 - j. Have you been coughing a lot lately?

2. Past and family histories

- a. Past history of congenital or acquired heart disease, cardiac surgery, asthma, or Kawasaki disease
- b. Medications, such as asthma medicines or birth control pills
- c. Family history of recent chest pain or a cardiac death
- d. Family history of long QT syndrome, cardiomyopathies, or unexpected sudden death
- e. History of exposure to drugs (cocaine) or cigarettes

3. Physical examination

- a. The chest wall should be carefully examined for trauma, asymmetry, and costochondritis.
 - (1) For costochondritis, use the soft part of the terminal phalanx of a middle finger (not the palm of a hand) to palpate each costochondral and chondrosternal junction.
 - (2) Pectoralis muscles and shoulder muscles should be examined for tenderness.
 - (3) Chest wall deformities (scoliosis, kyphosis, or pectus) can be a cause of chronic chest pain.
- b. The abdomen should be carefully examined, because it may be the source of pain referred to the chest.
- c. The heart and lungs should be auscultated for arrhythmias, heart murmurs, rubs, muffled heart sounds, gallop rhythm, crackles, wheezes, or decreased breath sounds. One must be careful not to interpret commonly occurring innocent murmurs as pathologic.

4. Other investigations

- a. Chest radiographs (for pulmonary pathology, cardiac size and silhouette, and pulmonary vascularity) may be obtained.
- b. An ECG (for arrhythmias, hypertrophy, conduction disturbances, WPW preexcitation, and prolonged QT intervals) may be obtained.
- c. Drug screening is ordered when cocaine-induced chest pain is suspected.

III. STEPPED APPROACH TO DIAGNOSIS

The stepped approach to diagnosis as described in the following section may be used in dealing with children with a complaint of chest pain.

1. The first step is to search for three common noncardiac causes of chest pain: costochondritis, musculoskeletal causes, and respiratory diseases. History and physical examination frequently uncover one of these conditions as the cause of chest pain in about two thirds of patients.
2. The second step is to evaluate for possible cardiac causes of the pain. Even if a noncardiac cause of the pain is found, cardiac causes of pain should still be looked into because the final goal is to rule out cardiac causes of chest pain. It is relatively easy to rule out cardiac causes of chest pain by history and physical examination (see [Table 20-2](#)). The following lists some relevant facts about chest pain of cardiac origin.
 - a. Cardiac cause of chest pain is usually typical anginal pain.
 - (1) The patient describes the pain as a deep, heavy pressure; the feeling of choking; or a squeezing sensation. It is not sharp pain of short duration. The pain is located in the precordial or substernal area and may radiate to the neck, jaw, either or both arms, back, or abdomen.
 - (2) Exercise, heavy physical activities, or emotional stress typically precipitates the cardiac pain. Nonexertional pain is unlikely of cardiac origin, with the exception of pleural pain (which changes with position of the body and respiration).
 - (3) Associated symptoms such as syncope, dizziness, or palpitation suggest potential cardiac origin of the pain.
 - b. Chest pain of noncardiac origin is likely when many of the following are found:
 - (1) Nonexertional pain, occurring while watching TV or sitting in class.
 - (2) Sharp pain of short duration.
 - (3) Pain of chronic nature.
 - (4) Negative past history for heart disease or Kawasaki disease.
 - (5) Negative family history for hereditary heart disease (such as long QT syndrome, cardiomyopathies, unexpected sudden death).
 - (6) No associated symptoms such as syncope, dizziness, or palpitation.
 - (7) Unremarkable cardiac examination.
 - (8) Normal ECG and chest radiographs.

3. If none of the three common noncardiac causes of chest pain is found and history and physical examination suggest a noncardiac cause of chest pain, the clinician can reassure the patient and family of the probable benign nature of the chest pain.
4. At this point, the physician may decide either to do a simple follow-up or to consider a condition in other systems, such as gastrointestinal (such as GE reflux, peptic ulcer), pulmonary (including exercise-induced asthma), or psychogenic origin. Simple follow-up often clarifies the cause or the pain may subside without recurrence.
5. Drug screening for cocaine may be worthwhile in adolescents who have acute, severe chest pain and distress with an unclear cause.
6. An appropriate referral to a specialist may be considered at this stage.

IV. REFERRAL TO A CARDIOLOGIST

The following are some of the indications for referral to a cardiologist for cardiac evaluation of chest pain:

1. When chest pain is triggered or worsened by physical activities or is accompanied by other symptoms such as palpitation, dizziness, or syncope.
2. When there are abnormal findings in the cardiac examination, or when abnormalities occur in the chest radiographs or ECG.
3. When there is a family history of cardiomyopathy, long QT syndrome, sudden unexpected death, or other hereditary diseases commonly associated with cardiac abnormalities.
4. High levels of anxiety in the family and patient and a chronic, recurring nature of the pain are also important reasons for referral to a cardiologist.

V. TREATMENT

When a specific cause of chest pain is identified, treatment is directed at correcting or improving the cause.

1. Costochondritis can be treated by reassurance and occasionally by nonsteroidal antiinflammatory agents (such as ibuprofen) or acetaminophen. Ibuprofen is a better choice because it is an antiinflammatory as well as analgesic agent.
 - a. Ibuprofen 5 to 10 mg/kg/dose, 3 to 4 times a day, for 7 days, often improves the pain. The same course may be repeated 2 to 3 times with a intervening one-week period of no medication.
 - b. Physical activities requiring the use of shoulder and arm muscles should be avoided, including sports using arms, push-ups, pull-ups, certain house chores, and others.
 - c. Weight of backpacks should be reduced to a minimum.
2. Most musculoskeletal and nonorganic causes of chest pain can be treated with rest, nonsteroidal antiinflammatory agents, or acetaminophen.
3. Exercise-induced asthma is most effectively prevented by inhalation of a β_2 -agonist 10 to 15 minutes before exercise. Inhaled albuterol usually affords protection for 4 hours.

4. If gastritis, gastroesophageal reflux, or peptic ulcer disease is suspected, trials of antacids, hydrogen ion blockers, or prokinetic agents (such as metoclopramide [Reglan]) are helpful therapeutically (as well as diagnostically).
5. If organic causes of chest pain are not found and psychogenic etiology is suspected, psychological consultation may be considered.
6. When cocaine-associated chest pain is suspected in an emergency room setting, follow recent guidelines from the American Heart Association (McCord et al, 2008).
 - a. If cocaine intoxication is suspected, benzodiazepines are recommended as the primary treatment for anxiety, tachycardia, and hypertension.
 - b. Aspirin and nitrates continue to be strongly recommended.
 - c. However, β -blockers (including agents with mixed α -adrenergic antagonist effects, such as labetalol) are considered contraindicated because the unopposed α -adrenergic effect leads to worsening coronary vasoconstriction and increasing blood pressure.
 - d. Calcium channel blockers are not recommended because they may increase mortality rates.
 - e. Early percutaneous coronary intervention is indicated if myocardial infarction is likely the diagnosis.

Chapter 21

Syncope

I. DEFINITION

The brain depends on a constant supply of oxygen and glucose for normal function. Significant alterations in the supply of oxygen and glucose to the brain may result in a transient loss of consciousness.

1. Syncope is a transient loss of consciousness and muscle tone with a fall.
2. Presyncope is the feeling that one is about to pass out but remains conscious with a transient loss of postural tone.
3. Dizziness is the most common prodromal symptom of syncope.

II. PREVALENCE AND CAUSES

1. As many as 15% of children and adolescents are estimated to have a syncopal event between the ages of 8 and 18 years.
2. Syncope may be due to noncardiac causes (usually autonomic dysfunction), cardiac conditions, neuropsychiatric disorders, and metabolic disorders. [Box 21-1](#) lists possible causes of syncope.
3. In adults, most cases of syncope are caused by cardiac problems.
4. In children and adolescents, most incidents of syncope are benign, resulting from vasovagal episodes (probably the most common cause), other orthostatic intolerance entities, hyperventilation, and breath holding.
5. Before age 6 years, syncope is likely caused by a seizure disorder, breath holding, or cardiac arrhythmias.

III. DESCRIPTION OF DIFFERENT CAUSES OF SYNCOPE

Only autonomic dysfunction (or noncardiac circulatory) and cardiac causes of syncope are presented; neurologic and metabolic causes are not discussed.

A. Noncardiac Causes (Autonomic Dysfunction)

1. **Orthostatic intolerance** encompasses disorders of blood flow, heart rate (HR), and blood pressure (BP) regulation that are most easily demonstrable during orthostatic stress. The recently popularized head-up tilt test has identified three entities: vasovagal syncope, orthostatic hypotension, and postural orthostatic tachycardia syndrome (POTS).
 - a. **Vasovagal syncope** (also called simple fainting or neurocardiogenic syncope).
 - (1) This is the most common type of syncope seen in otherwise healthy children and adolescents. It is uncommon before ages 10 to 12 but quite prevalent in adolescents, especially girls. It is characterized by a prodrome lasting a few seconds to a minute.

BOX 21-1**CAUSES OF SYNCOPE****AUTONOMIC (NONCARDIAC)**

Orthostatic intolerance group

Vasovagal syncope (also known as simple, neurocardiogenic, or neurally mediated syncope)

Orthostatic (postural) hypotension (dysautonomia)

Postural orthostatic tachycardia syndrome (POTS)

Exercise-related syncope (see further discussion in text)

Situational syncope

Breath holding, cough, micturition, defecation, etc.

Carotid sinus hypersensitivity

Excess vagal tone

CARDIAC

Arrhythmias

Tachycardias: SVT, atrial flutter/fibrillation, ventricular tachycardia (seen with long QT syndrome, arrhythmogenic RV dysplasia)

Bradycardias: Sinus bradycardia, asystole, complete heart block, pacemaker malfunction

Obstructive lesions

Outflow obstruction: AS, PS, hypertrophic cardiomyopathy, pulmonary hypertension

Inflow obstruction: MS, tamponade, constrictive pericarditis, atrial myxoma

Myocardial

Coronary artery anomalies, hypertrophic cardiomyopathy, dilated cardiomyopathy, MVP, arrhythmogenic RV dysplasia

NEUROPSYCHIATRIC

Hyperventilation

Seizure

Migraine

Tumors

Hysteria

METABOLIC

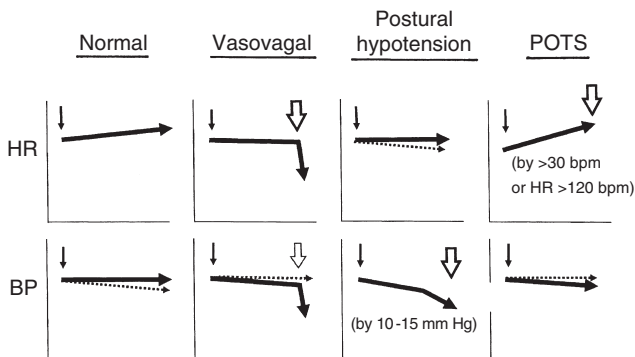
Hypoglycemia

Electrolyte disorders

Anorexia nervosa

Drugs/toxins

The prodrome may include dizziness, nausea, pallor, diaphoresis, palpitation, blurred vision, headache, and/or hyperventilation. The prodrome may be followed by the loss of consciousness and muscle tone with a fall. The unconsciousness does not last more than a minute. The syncope may occur after rising in the morning or in association with prolonged standing, anxiety or fright, pain, blood drawing or the sight of blood, fasting, hot and humid conditions, or crowded places. Typical response of patients with vasovagal syncope to the head-up tilt table test is precipitous drops in both the HR and BP (see Fig. 21-1).

**FIGURE 21-1**

Schematic drawing of changes in heart rate and blood pressure observed during the head-up tilt test. Thin arrows mark the start of orthostatic stress. Large unfilled arrows indicate appearance of symptoms with changes seen in heart rate (HR) and blood pressure (BP). POTS, postural orthostatic tachycardia syndrome. (From Park MK: *Park's Pediatric Cardiology for Practitioners*, ed 6, Philadelphia, Mosby, 2014.)

History is most important in establishing the diagnosis of vasovagal syncope.

(2) Proposed pathophysiology of vasovagal syncope.

- The normal responses to assuming an upright posture are a reduced cardiac output, an increase in heart rate, and an unchanged or slightly diminished systolic pressure with about 6% decrease in cerebral blood flow.
- Proposed pathophysiology of vasovagal syncope is as follows. In susceptible individuals, a sudden decrease in venous return to the ventricle produces a large increase in the force of ventricular contraction, which causes activation of the left ventricular mechanoreceptors. A sudden increase in neural traffic to the brain stem somehow mimics the conditions seen in hypertension and thereby produces a paradoxical withdrawal of sympathetic activity, which results in peripheral vasodilatation, hypotension, bradycardia, and subsequent decrease in cerebral perfusion. Hydration status affects the response; a dehydrated person is more likely to have syncope, while well-hydrated persons may not have it.

b. **Orthostatic hypotension (dysautonomia)**

- The normal response to standing is reflex arterial and venous constriction and a slight increase in heart rate. In orthostatic hypotension, the normal adrenergic vasoconstriction of the arterioles and veins in the upright position is absent or inadequate, resulting in hypotension without a reflex increase in HR (see Fig. 21-1). Unlike

the prodrome seen with vasovagal syncope, patients experience only lightheadedness in orthostatic hypotension. They do not display the autonomic nervous system signs seen with vasovagal syncope, such as pallor, diaphoresis, and hyperventilation. Prolonged bed rest, prolonged standing, dehydration, drugs that interfere with the sympathetic vasomotor response (e.g., calcium channel blockers, antihypertensive drugs, vasodilators, phenothiazines), and diuretics may exacerbate orthostatic hypotension.

- (2) In patients suspected of having orthostatic hypotension, BPs should be measured in the supine and standing positions. A fall in systolic/diastolic pressure of more than 20/10 mm Hg within 3 minutes of assuming the upright position without moving the arms or legs, with no increase in the heart rate but without fainting, suggests the diagnosis.

c. Postural orthostatic tachycardia syndrome (POTS)

- (1) This syndrome, most often observed in young women, is a form of autonomic neuropathy that predominantly affects the lower extremities. Venous pooling associated with assuming a standing position leads to a reduced venous return and a resulting increase in sympathetic discharge with a significant degree of tachycardia. Affected patients often complain of chronic fatigue, exercise intolerance, palpitation, lightheadedness, nausea, and recurrent near syncope (and sometimes syncope). These symptoms may be related to *chronic fatigue syndrome* and may be misdiagnosed as panic attacks or chronic anxiety. Occasional patients develop swelling of the lower extremities with purplish discoloration of the dorsum of the foot and ankle.
- (2) For the diagnosis of POTS, heart rate and blood pressure are measured in the supine, sitting, and standing positions. POTS is defined as the development of orthostatic symptoms that are associated with at least a 30 beat/minute increase in heart rate (or a heart rate of ≥ 120 beats/minute) that occurs within the first 10 minutes of standing or upright tilt, with occurrence of symptoms described previously (see Fig. 21-1).

2. **Exercise-related syncope.** Athletic adolescents may experience syncope or presyncope during or after strenuous physical activities. This may signal serious cardiac problems, but in most cases it occurs due to a combination of venous pooling in vasodilated leg muscles, inadequate hydration, and high ambient temperature. To prevent venous pooling, athletes should keep moving after running competitions. Secondary hyperventilation from exercise activities with resulting hypocapnia may also contribute to this form of syncope. Tingling or numbness of extremities may occur with hypocapnia.

3. Situational syncope.

- a. Micturition syncope is a rare form of orthostatic hypotension. In this condition, rapid bladder decompression results in decreased total

peripheral vascular resistance with splanchnic stasis and reduced venous return to the heart, resulting in postural hypotension.

- b. Cough syncope follows paroxysmal nocturnal coughing in asthmatic children. Paroxysmal coughing produces a marked increase in intrapleural pressure with a reduced venous return and reduced cardiac output, resulting in altered cerebral blood flow and loss of consciousness.

B. Cardiac Causes of Syncope

Cardiac causes of syncope may include obstructive lesions, myocardial dysfunction, and arrhythmias (see [Box 21-1](#)).

1. **Obstructive lesions.** Patients with severe AS, PS, or hypertrophic obstructive cardiomyopathy (HOCM), as well as those with pulmonary hypertension, may have syncope. Exercise often precipitates syncope associated with these conditions. These patients may also complain of chest pain, dyspnea, and palpitation.
2. **Myocardial dysfunction.** Although rare, myocardial ischemia or infarction secondary to congenital anomalies of the coronary arteries or acquired disease of the coronary arteries (such as Kawasaki disease, postsurgical, or atherosclerotic heart disease) may cause syncope.
3. **Arrhythmias.** Either extreme tachycardia or bradycardia can cause syncope. Commonly encountered rhythm disturbances include SVT, ventricular tachycardia (VT), sick sinus syndrome, and complete heart block. Imaging studies may or may not show structural abnormalities.
 - a. No identifiable structural defect is present in long QT syndrome, WPW syndrome, RV dysplasia, and Brugada syndrome.
 - b. Identifiable structural heart defects are imaged for the following conditions.
 - (1) Preoperative CHDs (such as Ebstein anomaly, MS, or MR, and L-TGA).
 - (2) Postoperative CHDs (such as TOF, TGA, after Fontan operation) may cause sinus node dysfunction, SVT, VT, or complete heart block.
 - (3) Dilated cardiomyopathy can cause sinus bradycardia, SVT, or VT.
 - (4) Hypertrophic cardiomyopathy is a rare cause of VT and syncope.

IV. EVALUATION OF A CHILD WITH SYNCOPÉ

A. History

Accurate history taking is most important in determining cost-effective diagnostic strategies.

1. About the syncopal event
 - a. The time of day: Syncope occurring after rising in the morning suggests vasovagal syncope. Hypoglycemia is a very rare cause of syncope.

- b. The patient's position: Syncope while sitting or recumbent suggests arrhythmias or seizures. Syncope after standing for some time suggests vasovagal syncope or other orthostatic intolerance group.
 - c. Relationship to exercise
 - (1) Syncope occurring during exercise suggests arrhythmias.
 - (2) Syncope occurring immediately after cessation of strenuous physical activities (such as football practice or game) may be due to venous pooling in the leg, and rarely due to arrhythmias. Vigorousness and duration of the activity, relative hydration status, and ambient temperature are important.
 - d. Associated symptoms
 - (1) Palpitation or racing heart rate suggests arrhythmia or tachycardia.
 - (2) Chest pain suggests possible myocardial ischemia (due to obstructive lesions, cardiomyopathy, carditis, etc.).
 - (3) Shortness of breath or tingling or numbness of extremities suggests hyperventilation.
 - (4) Nausea, epigastric discomfort, and diaphoresis suggest vasovagal syncope.
 - (5) Headache or visual changes also suggest vasovagal syncope.
 - e. The duration of syncope
 - (1) Syncopal duration less than 1 minute suggests vasovagal syncope, hyperventilation, or syncope due to other orthostatic mechanism.
 - (2) A longer duration of syncope suggests convulsive disorders, migraine, or cardiac arrhythmias.
 - f. The patient's appearance during and immediately following the episode.
 - (1) Pallor indicates hypotension.
 - (2) Abnormal movement or posturing, confusion, focal neurologic signs, amnesia, or muscle soreness suggests the possibility of seizure.
- 2. Past history of cardiac, endocrine, neurologic, or psychological disorders may suggest a disorder in that system.
 - 3. Medications, including prescribed, over-the-counter, and recreational drugs should be checked.
 - 4. Family history should include the following data:
 - a. Myocardial infarction in family members younger than 30 years of age.
 - b. Cardiac arrhythmia, CHD, cardiomyopathies, long QT syndrome, seizures, and metabolic and psychological disorders.
 - c. Positive family history of fainting is common in patients with vasovagal syncope.
 - 5. Social history is important in assessing whether there is a possibility of substance abuse, pregnancy, or factors leading to a conversion reaction.

B. Physical Examination

Although physical examination is usually normal, it should always be performed, focusing on the cardiac and neurologic systems.

1. Careful auscultation includes heart murmurs or abnormally loud second heart sounds.
2. If orthostatic intolerance group is suspected, the heart rate and BP should be measured repeatedly while the patient is supine and after standing without moving for up to 10 minutes.
3. Neurologic examination should include a fundoscopic examination, test for Romberg sign, gait evaluation, deep tendon reflexes, and cerebellar function.

C. Diagnostic Studies

History and physical examinations guide practitioners in choosing the diagnostic tests that apply to a given syncopal patient.

1. Serum glucose and electrolytes are of limited value, because the patients are seen hours or days after the episode.
2. When an arrhythmia is suspected as the cause of syncope:
 - a. The ECG should be inspected for heart rate (bradycardia), arrhythmias, WPW preexcitation, heart block, long QTc interval, and abnormalities suggestive of cardiomyopathies and myocarditis.
 - b. Ambulatory ECG monitoring (24-hour Holter monitor or event recorder) is usually obtained.
3. Echo studies are performed to rule out CHDs, pulmonary hypertension, and cardiomyopathies and to check on the status of postoperative CHDs.
4. Exercise stress test is indicated if the syncopal event is associated with exercise.
5. Rarely cardiac catheterization and electrophysiologic study may be indicated in some equivocal cases.
6. Head-up tilt table test. If patients with positional syncope have autonomic symptoms (such as pallor, diaphoresis, or hyperventilation), tilt table testing is sometimes performed by some centers (see following section).
7. Neurologic consultation. Patients who faint while sitting or recumbent and those who exhibit prolonged loss of consciousness, seizure activity, and a postictal phase with lethargy or confusion should be referred for neurologic consultation.

D. Head-Up Tilt Table Test

The goal of the test is to provoke the patient's symptoms during an orthostatic stress while closely monitoring the patient's cardiac rhythm, heart rate, and BP responses associated with symptoms. Orthostatic stress is created by a tilting table with the patient placed in an upright position for a certain period of time. Various protocols are available.

Positive responses commonly include lightheadedness, dizziness, nausea, visual changes, and frank syncope. Sinus bradycardia, junctional bradycardia, and asystole for as long as 30 seconds are common. Hypotension

generally is manifested by systolic blood pressures of less than 70 mm Hg. Returning the patient to the supine position produces resolution of symptoms rapidly, usually with a reactive tachycardia.

Although several distinct abnormal patterns have been identified during the head-up tilt table tests (as shown in Fig. 21-1), there are serious questions about the sensitivity, specificity, diagnostic yield, and day-to-day reproducibility of the tilt test. In adults, the overall reproducibility of syncope by the tilt test is disappointingly low (62%). About 25% of adolescents with no prior fainting history fainted during the tilt test. Moreover, among habitual fainters, 25% to 30% did not faint during the test on a given day.

V. TREATMENT

1. Orthostatic intolerance group. Regardless of the type, the same preventive measures are used for all orthostatic intolerance groups. Beginning the therapy empirically without performing a head-up tilt table test is not unreasonable.
 - a. The patient is advised to avoid extreme heat and dehydration and to increase salt and fluid intake.
 - b. β -Blocker therapy is used commonly, especially in adolescents and young adults, to modify the feedback loop. Atenolol (1-1.2 mg/kg/day PO QD, max dose 2 mg/kg/day) or metoprolol (1.5 mg/kg/day given PO in two or three doses) is most commonly used.
 - c. α -Agonist therapy using pseudoephedrine (60 mg, PO, BID) or an ephedrine-theophylline combination (Marax) stimulates the heart rate and increases the peripheral vascular tone, preventing reflex bradycardia and vasodilation.
 - d. Fludrocortisone (Florinef), a mineralocortisone, 0.1 mg PO, QD or BID for children; 0.2 mg/day for adults, with increased salt intake or a salt tablet (1 g daily) may be tried. Average children commonly gain 1 kg or 2 kg water weight into their circulating volume within 2 or 3 weeks.
2. Cardiac arrhythmias presenting as syncopal events require antiarrhythmic therapy or radiofrequency ablation (see treatment for specific arrhythmias in Chapter 16).

VI. DIFFERENTIAL DIAGNOSIS OF SYNCOPES

1. Epilepsy. Patients with epilepsy may have incontinence, marked confusion in the postictal state, and abnormal electroencephalograms (EEGs). Patients are rigid rather than limp and may have sustained injuries. Patients do not experience the prodromal symptoms of syncope (e.g., dizziness, pallor, palpitation, and diaphoresis). The duration of unconsciousness is longer than that typically seen with syncope (<1 minute).
2. Hypoglycemia. Hypoglycemic attacks differ from syncope in that the onset and recovery occur more gradually, and they do not occur during or shortly after meals.

3. Hyperventilation. Hyperventilation produces hypocapnia, which in turn produces intense cerebral vasoconstriction, causing syncope. It may also have a psychological component. The patient often experiences air hunger, shortness of breath, chest tightness, abdominal discomfort, palpitations, dizziness, and numbness or tingling of the face and extremities, and rarely loss of consciousness. The syncopal episode can be reproduced in the office when the patient hyperventilates.
4. Hysteria. Syncope resulting from hysteria is not associated with injury and occurs only in the presence of an audience. During these attacks, the patient does not experience the pallor and hypotension that characterize true syncope. The attacks may last longer (up to an hour) than a brief syncopal spell. Episodes usually occur in an emotionally charged setting and are rare before 10 years of age.

Chapter 22

Palpitation

I. DEFINITION

Palpitation is one of the most common cardiac symptoms encountered in medical practice but it poorly corresponds to demonstrable abnormalities. The term *palpitation* is used loosely to describe an unpleasant subjective awareness of one's own heartbeats. This usually occurs as a sensation in the chest of rapid, irregular, or unusually strong heartbeats.

II. CAUSES

Many palpitations are often not serious, but they may indicate the possible presence of serious cardiac arrhythmias. [Box 22-1](#) lists causes of palpitation.

1. A high percentage of patients with palpitation have no etiology that can be established.
2. Certain stimulants, such as caffeine, can be identified as a cause of palpitation. Caffeine is found in many foods and drinks, such as coffee, tea, hot cocoa, soda, and chocolate, and some medicines. Most energy drinks (such as Venom, Whoopass, Red Bull, Adrenalin Rush) contain large doses of caffeine and other legal stimulants including ephedrine, guarana, taurine, and ginseng.
3. Certain drugs, prescription or over-the-counter, can be identified as a cause of palpitation.
4. Some medical conditions, such as hyperthyroidism, anemia, and hypoglycemia, may be the cause of palpitation.
5. Rarely, slow heart rates may cause palpitation.
6. Some patients report palpitation while having sinus tachycardia.
7. Rarely cardiac arrhythmias should be looked into as a cause of palpitation, although most arrhythmias are not perceived and reported as palpitations.
8. Occasionally, a psychogenic or psychiatric cause for the symptoms can be suspected. Some adult patients with palpitations have panic disorder or panic attack.

III. EVALUATION

A. History

1. The nature and onset of palpitation may suggest causes.
 - a. Isolated “jumps” or “skips” suggest premature beats.
 - b. Sudden start and stop of rapid heartbeat or a pounding of the chest suggests SVT. Some children will appear sweaty or pale with SVT.

BOX 22-1**CAUSES OF PALPITATION**

Normal physiologic event

Exercise, excitement, fever

Psychogenic or psychiatric

Fear, anger, stress, anxiety disorders, panic attack or panic disorder

Certain drugs and substances

Stimulants: caffeine (coffee, tea, soda, chocolate), some energy drinks, smoking

Over-the-counter drugs: decongestants, diet pills, etc.

Drugs that cause tachycardia: catecholamines, theophylline, hydralazine, minoxidil, cocaine

Drugs that cause bradycardia: β -blockers, antihypertensive drugs, calcium channel blockers

Drugs that cause arrhythmias: antiarrhythmics (some of which are proarrhythmic), tricyclic antidepressants, phenothiazines

Certain medical conditions

Anemia

Hyperthyroidism

Hypertension

Pheochromocytoma (with catecholamine excess)

Hypoglycemia

Hyperventilation

Poor physical condition

Heart diseases

Certain CHDs that are prone to arrhythmias or result in poor physical condition

Following surgeries for CHD: Fontan connection, Senning operation

Mitral valve prolapse

Hypertrophic cardiomyopathy

Dilated cardiomyopathy

Cardiac tumors or infiltrative diseases

Cardiac arrhythmias

Tachycardias: sinus tachycardia, SVT, VT

Bradycardia

Premature beats: PACs, PVCs

Atrial fibrillation

Sick sinus syndrome

CHD, congenital heart defect; PACs, premature atrial contractions; PVCs, premature ventricular contractions; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

- c. A gradual onset and cessation of palpitation suggest sinus tachycardia or anxiety state.
 - d. Palpitation characterized by slow heart rate may be due to atrioventricular (AV) block or sinus node dysfunction.
2. Relationship to exertion
- a. A history of palpitation during strenuous physical activity may be a normal phenomenon (due to sinus tachycardia), although it could be due to exercise-induced arrhythmias.

- b. Nonexertional palpitation may suggest atrial flutter/fibrillation, febrile state, thyrotoxicosis, hypoglycemia, or anxiety state.
- c. Palpitation on standing suggests postural hypotension.
- 3. Associated symptoms
 - a. Symptoms of dizziness or fainting associated with palpitation may indicate ventricular tachycardia.
 - b. The presence of other symptoms, such as chest pain, sweating, nausea, or shortness of breath, may increase the likelihood of identifiable causes of palpitation.
- 4. Personal and family history
 - a. Caffeine-containing drinks (such as coffee, tea, hot cocoa, chocolates, and energy drinks)
 - b. Prescription and over-the-counter medications
 - c. Family history of syncope, sudden death, or arrhythmias

B. Physical Examination

- 1. Most children with palpitation have normal physical examinations, except for those with hyperthyroidism.
- 2. Cardiac examination may reveal findings of MVP, obstructive lesions, or possibly cardiomyopathy.

C. Recording of ECG Rhythm

Recording of ECG rhythm that coincides with the timing of the patient's complaint of palpitation is a certain way of making diagnosis of arrhythmia or ruling it out as the cause of palpitation. A number of ECG recording techniques are available.

- 1. Routine ECG may show prolonged QTc interval, delta waves (WPW preexcitation), or AV block.
- 2. When palpitation occurs almost daily, a 24-hour Holter monitoring is usually most helpful in making the diagnosis of the rhythm abnormality. Some children actually complain of palpitation during sinus tachycardia.
- 3. When palpitation occurs infrequently, long-term event monitor recording (up to 30 days) is indicated. With infrequent palpitations that are fairly long-lasting, hand-held or patient-activated nonlooping memory event recorders are indicated. However, with infrequent short-lasting palpitation, external loop recorders are indicated.
- 4. Implantable loop recorders (inserted under the skin at about the second rib on the left front of the chest) can be used to monitor for a period longer than one month (may be up to a year). These can be worn during swimming or other vigorous exercises.
- 5. Continuous outpatient telemetry monitoring is a new monitoring modality available at most tertiary care facilities. The patient is fitted with a transmitter which sends the ECG data to the area of the hospital where the telemetry monitoring occurs. The patient can move around within the device's transmitting range.

D. Echocardiography

Echo studies help identify structural heart disease, such as cardiomyopathies, cardiac tumors, MVP, and other structural abnormalities of the heart.

E. Exercise Stress Test

If the symptoms occur during exercise, an exercise stress test may be helpful in making the diagnosis.

F. Laboratory Studies

When other medical conditions are suspected as a cause of palpitation, full blood count (for anemia), electrolytes, blood glucose, and thyroid function testing may be indicated.

G. Electrophysiology

If there is a high suspicion of ventricular tachycardia, sometimes provocative electrophysiologic studies may be indicated.

IV. MANAGEMENT

1. If the rhythm recorded on the 24-hour Holter monitoring shows sinus tachycardia at the time of the complaint of palpitation, reassure the parent and child of the normal, benign nature of palpitation.
2. Stimulant-containing drinks (coffee, tea, hot cocoa, chocolate, sodas, and energy drinks) should be reduced or eliminated.
3. Treat medical causes of palpitation (such as hyperthyroidism), if present.
4. Examination of all medications that the patient is taking may be helpful in the diagnosis, in modifying the dosage or schedule, or changing to other medications.
5. For isolated PACs or PVCs, nothing needs to be done except avoidance of stimulants such as those listed previously.
6. If a significant cardiac arrhythmia or an AV conduction disturbance is found, appropriate therapy should be given for the conditions found.
7. If palpitation is associated with symptoms, such as fainting, dizziness, chest pain, pallor, or diaphoresis, further evaluation is guided as described under syncope or chest pain.

Chapter 23

Systemic Hypertension

1. DEFINITION

A. For Adults

1. Blood pressure (BP) levels lower than 120/80 mm Hg are now considered normal.
2. A BP level of 120/80 mm Hg, previously considered normal, is now classified as prehypertension.
3. Hypertension is further classified as stage 1 and stage 2 depending on the level of abnormalities (see [Table 23-1](#)).

B. For Children

1. Prehypertension is defined as an average systolic and/or diastolic pressure between the 90th and 95th percentiles for age and gender.
2. Hypertension is defined as systolic and/or diastolic pressure levels that are greater than the 95th percentile for age and gender or $\geq 120/80$ mm Hg as in adults on at least three occasions.
3. Hypertension is further classified into stages 1 and 2 as follows.
 - a. Stage 1 hypertension is present when BP readings are between the 95th and 99th percentiles.
 - b. Stage 2 hypertension is present when BP readings are 5 mm Hg or more above the 99th percentile values (see [Table 23-1](#)).
4. “White-coat hypertension” is present when BP readings in health care facilities are in hypertensive ranges but readings are normotensive outside a clinical setting.

II. NORMATIVE BP STANDARDS

1. The BP Tables provided by the Working Group of the National High Blood Pressure Education Program (NHBPEP) are not acceptable standards because they are obtained by a methodology currently unacceptable and are discordant from their own recommendations, statistically unsound, and impractical for practitioners (as discussed in Chapter 1).
2. Normative BP standards from the San Antonio Children’s Blood Pressure Study (SACBPS) are the most reliable sets; they are the only large sets of BP standards obtained using the currently recommended methodology. In that study, both auscultatory and oscillometric (Dinamap 800) methods were used.
 - a. The auscultatory BP standards for children 5 to 17 years old are shown in Tables B-3 and B-4, in Appendix B.
 - b. A different set of BP standards is needed for the oscillometric method because BP readings by Dinamap Monitor Model 8100, a popular

TABLE 23-1
CLASSIFICATION OF BLOOD PRESSURE FOR ADULTS AND CHILDREN

BP CLASSIFICATION	Adults (mm Hg)*		CHILDREN AND ADOLESCENTS†
	SYSTOLIC BP	DIASTOLIC BP	
Normal	<120	<80	<90th percentile
Prehypertension	120-139	80-89	90th-95th percentile
Stage 1 hypertension	140-159	90-99	95th-99th percentile
Stage 2 hypertension	≥160	≥100	>5 mm Hg + 99th percentile

*Adapted from Chobanian AV et al: The 7th report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report, JAMA 21:2560-2572, 2003.

†Pediatric classification is according to the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents, Pediatrics 111:555-576, 2004.

oscillometric device, are significantly different from those obtained by the auscultatory method. Dinamap readings are on average 10 mm Hg higher for the systolic pressure and 5 mm Hg higher for the diastolic pressure than readings using the auscultatory method.

- (1) Normative oscillometric BP standards for children 5 to 17 years old from the SACBPS are presented in Tables B-5 and B-6, in Appendix B.
- (2) Oscillometric BP standards for neonates and small children up to 5 years of age are presented in Table 1-3.
3. Recently, Kaelber et al (2009) have recommended a simplified table of BP levels according to age and gender (without height percentiles), above which further evaluation should be carried out for possible hypertension (the left half of Table 23-2). These BP values agree closely with the 90th percentile of the normative auscultatory BP standards from the SACBPS (Park et al, 2005).
4. Similarly, the oscillometric (Dinamap) BP levels above which further evaluation should be carried out for possible hypertension are presented in the right half of Table 23-2. These values are close to the 90th percentile normative values from the SACBPS.

III. CAUSES

1. With the increasing prevalence of obesity in recent decades, overweight and obesity have become the most common causes of pediatric hypertension.
2. More than 90% of secondary hypertension in nonobese children is caused by three conditions: renal parenchymal disease, renal artery disease, and coarctation of the aorta (COA).
3. In general, children with essential hypertension are older than 10 years of age, have mild hypertension, and often are obese.
4. Children with secondary hypertension are generally younger than 10 years of age and have higher levels of BP. Children with secondary hypertension rarely are obese and often are less than normal height.

TABLE 23-2**BLOOD PRESSURE VALUES REQUIRING FURTHER EVALUATION, ACCORDING TO AGE AND GENDER**

Auscultatory ^a					Oscillometric ^b				
Age (yr)	Male		Female		Age (yr)	Male		Female	
	SYST	DIAST	SYST	DIAST		SYST	DIAST	SYST	DIAST
3	100	59	100	61	3				
4	102	62	101	64	4				
5	104	65	103	66	5	116	70	115	69
6	105	68	104	68	6	118	70	116	69
7	106	70	106	69	7	119	70	117	70
8	107	71	108	71	8	120	71	119	70
9	109	72	110	72	9	122	71	120	71
10	111	73	112	73	10	123	72	122	71
11	113	74	114	74	11	125	72	123	72
12	115	74	116	75	12	128	72	124	72
13	117	75	117	76	13	130	72	126	73
14	120	75	119	77	14	130	73	126	73
15	120	76	120	78	15	130	73	127	74
16	120	78	120	78	16	130	73	127	74
17	120	80	120	78	17	130	73	127	74
≥18	120	80	120	80					

^aFrom Kaelber DC et al: Simple table to identify children and adolescents needing further evaluation of blood pressure, Pediatrics 123(6):e972, 2009. For adolescents 14 years and older, systolic pressure of 120 mm Hg is in prehypertensive range, as in adults.

^bFrom Park MK, et al: Oscillometric blood pressure standards for children, Pediatric Cardiology 26:601-607, 2005.

TABLE 23-3**COMMON CAUSES OF CHRONIC HYPERTENSION ACCORDING TO AGE**

AGE GROUP	CAUSES
Newborns	Renal artery thrombosis, renal artery stenosis, congenital renal malformation, COA, bronchopulmonary dysplasia (transient)
<6 yr	Renal parenchymal disease, COA, renal artery stenosis
6-10 yr	Renal artery stenosis, renal parenchymal disease, COA
>10 yr	Primary hypertension, renal parenchymal disease

COA, coarctation of the aorta.

Adapted from Report of the Second Task Force on Blood Pressure Control in Children, Pediatrics 79:1-25, 1987.

5. Table 23-3 lists the common causes of hypertension by age group in (nonobese) children. Box 23-1 lists causes of secondary hypertension.

IV. DIAGNOSIS OF HYPERTENSION

A. Steps in Diagnosis of Hypertension

Diagnosis of hypertension is not simple and easy. There are many factors that contribute to the erroneous diagnosis of hypertension in children and in adults. Careless, erroneous diagnosis of hypertension can lead to costly investigation

BOX 23–1**CAUSES OF SECONDARY HYPERTENSION****RENAL**

Renal parenchymal disease

Glomerulonephritis, acute and chronic

Pyelonephritis, acute and chronic

Congenital anomalies (polycystic or dysplastic kidneys)

Obstructive uropathies (hydronephrosis)

Hemolytic-uremic syndrome

Collagen disease (periarteritis, lupus)

Renal damage from nephrotoxic medications, trauma, or radiation

Renovascular disease

Renal artery disorders (e.g., stenosis, polyarteritis, thrombosis)

Renal vein thrombosis

CARDIOVASCULAR

Coarctation of the aorta

Conditions with large stroke volume (patent ductus arteriosus, aortic insufficiency, systemic arteriovenous fistula, complete heart block) (these conditions cause only systolic hypertension)

ENDOCRINE

Hyperthyroidism (systolic hypertension)

Excessive catecholamine levels

Pheochromocytoma

Neuroblastoma

Adrenal dysfunction

Congenital adrenal hyperplasia

- 11- β -hydroxylase deficiency
- 17-hydroxylase deficiency

Cushing syndrome

Hyperaldosteronism

- Primary

Conn's syndrome

Idiopathic nodular hyperplasia

Dexamethasone-suppressible hyperaldosteronism

- Secondary

Renovascular hypertension

Renin-producing tumor (juxtaglomerular cell tumor)

Hyperparathyroidism (and hypercalcemia)

NEUROGENIC

Increased intracranial pressure (any cause, especially tumors, infections, trauma)

Poliomyelitis

Guillain-Barré syndrome

Dysautonomia (Riley-Day syndrome)

DRUGS AND CHEMICALS

Sympathomimetic drugs (nose drops, cough medications, cold preparations, theophylline)

Amphetamines

BOX 23-1**CAUSES OF SECONDARY HYPERTENSION** (Continued)**DRUGS AND CHEMICALS** (Continued)

Corticosteroids
 Nonsteroidal antiinflammatory drugs
 Oral contraceptives
 Heavy-metal poisoning (mercury, lead)
 Cocaine, acute or chronic use
 Cyclosporine
 Thyroxine
 Tacrolimus

MISCELLANEOUS

Hypervolemia and hypernatremia
 Stevens-Johnson syndrome
 Bronchopulmonary dysplasia (newborns)

and even treatment using drugs, some of which may have irreversible side effects. The following issues must be considered in making the diagnosis of hypertension. After the diagnosis is confirmed the clinician must proceed with workups to find the cause of hypertension: primary or secondary.

1. One must use correct BP measurement techniques and compare the reading with reliable BP standards.
2. BP readings measured by the auscultatory and oscillometric methods are significantly different and thus not interchangeable; one must use BP standards specific for the method used.
3. White-coat hypertension further complicates the issue as the prevalence of white-coat hypertension in children and adolescents is estimated to be about 30% to 50%. Therefore, one must make efforts to confirm elevated BP readings outside the health care facilities.
4. In addition, one must confirm *persistently* elevated BP levels at least on three consecutive examinations.

B. What to Do When a High BP Reading Is Obtained in the Office

The following is one way of handling a case of high BP readings in the office setting.

1. If an abnormal reading is the result of single reading, obtain two additional readings.
2. If BP is still high, a repeat set of three readings is obtained at the end of the office visit, and readings are compared with a reliable BP standard, such as those from the SACBPS (see Tables B-3, B-4, B-5, and B-6 in Appendix B).
3. If BP readings are still high at the end of the office visit, a possibility of white-coat hypertension still exists. Consider ways to identify cases of white-coat hypertension by measuring BPs outside the health care facility.

- a. Some physicians advocate the use of the ambulatory BP (ABP) measurement to rule out white-coat hypertension. ABP measurement is costly and it reflects BP readings on a single day; BP readings vary from day to day.
 - b. Having reliable school nurses take daily BP for 2 to 4 weeks may be a cost-effective way to get the same information.
 - c. Home BP monitoring can be an option. It is reasonable to try home BP measurement in children under certain circumstances. However, objectivity and conflict of interest of the patient and/or parents should be considered before using this approach. An average of two (or three) BP readings taken in the morning and at night for 1 week (with a total of at least 12 readings) is recommended. For home BP monitoring, the monitor should be checked for its accuracy and the patient should be taught correct measurement technique and correct BP cuff size. Wrist monitors are not acceptable because the readings are expected to be higher due to peripheral amplification of systolic pressure. In evaluating home BP readings, it may be more reasonable to use the oscillometric BP standards, because most home BP devices use the oscillometric method rather than the auscultatory standards.
4. If a reliable BP measurement outside the doctor's office cannot be arranged, serial BP measurement (more than 10) can be obtained in the doctor's office by the same friendly staff to minimize white-coat effect.
 5. If multiple BP readings obtained outside the health care facility or in the doctor's office show persistently elevated BP levels above the 95th percentile most of the time, a tentative diagnosis of hypertension may be made, and initial investigation begun for the cause hypertension (as described in the following section).
 6. If the repeated BP measurements fall between the 90th and 95th percentiles (prehypertension), the patient should be followed on a regular basis (every 3 to 6 months) with repeat BP measurements.
 7. Even with the diagnosis of white-coat hypertension the patient should not be dismissed from follow-up. White-coat hypertension may not be as benign as it was once thought to be. Several recent studies in adults and children suggest that about 30% to 40% of patients with white-coat hypertension spontaneously evolve into hypertension, with accompanying end-organ damage. Thus, white-coat hypertension can be considered a prehypertension and patients should have several follow-ups before they are labeled as hypertensive or dismissed as normotensives. Some of these patients may need additional investigations as described for patients with established hypertension (see the following section).

V. EVALUATION FOR CAUSES OF HYPERTENSION

Evaluate the history (present, past, and family), perform a careful physical examination, and proceed with the initial investigation to look

for the cause of hypertension, as outlined in the section to follow. In general, children younger than 10 years of age with sustained hypertension require extensive evaluation, because identifiable and potentially curable causes are more likely to be found. Adolescents with mild hypertension and a positive family history of hypertension are more likely to have essential hypertension, and extensive studies are not indicated.

A. History

1. Neonatal: use of umbilical artery catheters or bronchopulmonary dysplasia.
2. History of palpitation, headache, and excessive sweating (signs of excessive catecholamine levels).
3. Renal: history of obstructive uropathies, urinary tract infection, and radiation, trauma, or surgery to the kidney area.
4. Cardiovascular: history of COA or surgery for it.
5. Endocrine: weakness and muscle cramps (hypokalemia seen with hyperaldosteronism).
6. Medications: corticosteroids, amphetamines, antiasthmatic drugs, cold medications, oral contraceptives, nephrotoxic antibiotics, cyclosporine, cocaine use.
7. Family history of essential hypertension, atherosclerotic heart disease, and stroke.
8. Familial or hereditary renal disease (polycystic kidney, cystinuria, familial nephritis).

B. Physical Examination

1. Accurate measurement of BP is essential.
2. Physical examination should focus on delayed growth (renal disease), bounding peripheral pulse (PDA or AR), weak or absent femoral pulses or BP differential between the arms and legs (COA), abdominal bruits (renovascular), and tenderness over the kidney (renal infection).
3. Children's weight and body mass index (BMI) percentile (obesity-related hypertension).

C. Laboratory and Other Investigations

1. Initial laboratory tests should be directed toward detecting renal parenchymal disease, renovascular disease, and COA. Therefore, tests should include urinalysis; urine culture; and serum electrolyte, blood urea nitrogen, creatinine, and uric acid levels. The ECG, chest radiographs, and possibly echo study may be useful (see [Table 23-4](#)).
2. When overweight is the likely cause of hypertension, metabolic aspects of risk factors should be checked.
3. More specialized studies may be indicated for the detection of rare causes of secondary hypertension ([Table 23-4](#)).

TABLE 23-4

ROUTINE AND SPECIAL LABORATORY TESTS AND THEIR SIGNIFICANCE

LABORATORY TEST	SIGNIFICANCE
Urinalysis, urine culture, blood urea nitrogen, creatinine, uric acid	Renal parenchymal disease
Serum electrolytes (hypokalemia)	Hyperaldosteronism (primary or secondary) Adrenogenital syndrome Renin-producing tumors
ECG, chest radiography, and possibly echocardiography	Cardiac cause of hypertension; also baseline function
Intravenous pyelogram (or ultrasonography, radionuclide studies, computed tomography, or magnetic resonance imaging of the kidneys)	Renal parenchymal disease Renovascular hypertension Tumors (neuroblastoma, Wilms tumor)
Plasma renin activity (peripheral)	High-renin hypertension (renovascular hypertension, renin-producing tumors, some Cushing syndrome, some essential hypertension) Low-renin hypertension (adrenogenital syndrome, primary hyperaldosteronism)
24-hr urine collection for 17-ketosteroid and 17-hydroxycorticosteroids	Cushing syndrome Adrenogenital syndrome
24-hr urine collection for catecholamine levels and vanillylmandelic acid	Pheochromocytoma Neuroblastoma
Aldosterone	Hyperaldosteronism (primary or secondary) Renovascular hypertension Renin-producing tumors
Renal vein plasma renin activity	Unilateral renal parenchymal disease Renovascular hypertension
Abdominal aortogram	Renovascular hypertension Abdominal coarctation of the aorta Unilateral renal parenchymal disease Pheochromocytoma
Intraarterial digital subtraction angiography	Renovascular hypertension

VI. MANAGEMENT OF HYPERTENSION

A. Nonpharmacologic Intervention

When the diagnosis of hypertension is established, nonpharmacologic intervention should be started as an initial treatment, as outlined in the following.

1. Counseling on weight reduction, if indicated;
2. Low-salt (and potassium-rich) foods;
3. Regular aerobic exercise; and
4. Avoidance of smoking and oral contraceptives.

B. Pharmacologic Intervention

1. **Indications for drug therapy.** Drugs are used when the nonpharmacologic approach is not effective. Although there are no clear guidelines,

the following are generally considered indications for initiating drug therapy in hypertensive children:

- a. Persistent hypertension (stage 1 or 2) despite nonpharmacologic measures (lifestyle changes).
 - b. Significant secondary hypertension (e.g., renovascular and renoparenchymal diseases).
 - c. Hypertension (stage 1 or 2) with target organ damage. The most reliable end-organ damage appears to be the presence of LVH evidenced by echo studies. Increased LV mass by echo may be an indication of LV hypertrophy but the values are not very reproducible and controversies exist as to how to express LV mass.
 - d. Hypertension (stage 1 or 2) with the presence of other risk factors for CV disease (dyslipidemia, diabetes, etc.).
 - e. Family history of early complications of hypertension.
 - f. Symptomatic hypertension, such as seen with acute glomerulonephritis (with intravenous antihypertensive medications).
2. **The choice of drug.** Recent studies in adults suggest that β -blockers are not as effective as other classes of antihypertensive agents. Currently, many adult cardiologists, especially those from European countries, strongly favor using angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), or calcium channel blockers (CCBs) as the drugs of choice for initial therapy. Some pediatric authorities recommend the same.
- a. Diuretics and β -blockers are known to raise blood glucose levels. Thus, CCBs and ACE inhibitors appear preferable to β -blockers and diuretics, especially for overweight patients at risk of developing diabetes.
 - b. ACE inhibitors and ARBs are good choices in patients with diabetes or renal disease because they are especially renoprotective.
 - c. CCBs may be a better choice for female adolescents because ACE inhibitors and ARBs are teratogenic.
 - d. For adolescent males:
 - (1) ACE inhibitors (or ARBs) and CCBs, alone or in combination, are equally good, especially in obese children with high glucose and triglyceride levels.
 - (2) ACE inhibitors + diuretics is a good combination because diuretics enhance ACE inhibitors' effects. However, this combination is not recommended in obese patients with acanthosis nigricans because it could cause diabetes.
 - e. For adolescent females or child-bearing-age women.
 - (1) CCBs (such as amlodipine [Norvasc] or extended release nifedipine) are good choices in females because they lack teratogenic effects.
 - (2) ACE inhibitors or ARBs should not be used in female adolescents because they are known teratogens.
 - (3) Diuretics or β -blockers are probably safe. However, blood glucose levels should be checked regularly because they raise glucose levels.

f. **Coexisting conditions.** The choice of initial therapy is influenced by other conditions that frequently coexist with hypertension. Preferences, contraindications, and side effects of different classes of antihypertensive agents are summarized in [Table 23-5](#), based on the information derived from adult experiences.

- (1) Migraine patients: β -blockers or CCBs are preferred. β -blockers appear to be more effective than CCBs in prevention of migraines.
- (2) Asthma: CCBs may be the drugs of first choice. ARBs and diuretics may work well. ACE inhibitors may cause persistent dry cough in 10% of 20% of patients with asthma and this may possibly cause bronchospasm. β -blockers are contraindicated in patients with asthma because they may cause bronchospasm.

TABLE 23-5

CLASSES OF ANTIHYPERTENSIVE AGENTS: PREFERENCES, CONTRAINDICATIONS, AND SIDE EFFECTS

DRUG CLASSES	PREFERRED	CONTRAINDICATED (NOT TO USE IN)	ADVERSE EFFECTS
Thiazide diuretics	Asthma (\pm)	<i>Not to use in:</i> Diabetic or prediabetic (It increases glucose level)	Hypokalemia, hyponatremia (\pm) May increase glucose May increase uric acid
β -blockers	Migraine Hyperthyroidism Hyperdynamic hypertension Coarctation of the aorta	<i>Contraindicated in:</i> Asthma and diabetes <i>Not to use in:</i> Prediabetic patients	Increases glucose Increases triglycerides Rarely hypoglycemia
ACE inhibitors (ACEI)	Male adolescents Diabetic or prediabetic Obese males (may be used in combination with CCB-Lotrel) Renal failure	<i>Contraindicated in:</i> Pregnancy (due to teratogenic effects) <i>Not to use in:</i> Child-bearing aged females Patients with asthma (can cause cough)	Hyperkalemia Azotemia Angioedema Dry cough Rash, loss of taste, and leukopenia
Angiotensin receptor blockers (ARB)	Male adolescents Diabetic or prediabetic Renal failure	<i>Contraindicated in:</i> Pregnancy (due to teratogenic effects) <i>Not to use in:</i> Child-bearing aged females	Angioedema rarely (but no cough)
Calcium channel blockers (CCB)	Female adolescents Male adolescents African Americans Migraine Asthma Renal failure	<i>Contraindicated in:</i> Heart block	Occasional headache, flushing, ankle edema

- (3) Hyperthyroidism or hyperdynamic hypertension with fast heart rates: β -blockers are preferred.
- (4) Diabetic patients: ACE inhibitors or ARBs are preferred. Thiazide diuretics or β -blockers should not be used because they increase blood glucose levels.
- (5) Renal failure: CCBs or ACE inhibitors are preferred.

C. Follow-Up

1. Once the most appropriate agent for initial therapy has been selected, a relatively small dose of a single drug should be started, aiming for BP reduction of 5 to 10 mm Hg at each step of the dosage, until the full dosage or the target BP is reached (see following).
2. If the first drug is not effective, a second drug may be added to, or substituted for, the first drug.
3. In many situations, however, more than one drug is needed to control severely elevated BPs like those seen in patients with renal disease, and thus starting with a combination of two drugs from classes with complementary mechanisms of action may be acceptable.
4. Single daily dose of a long-acting agent improves adherence to the medication. Long-acting preparations are available within each class of antihypertensive drug. [Table 23-6](#) shows the dosage of antihypertensive drugs for children.
5. The goal of the treatment.
 - a. For children with uncomplicated primary hypertension without hypertensive end-organ damage, the goal of the treatment is reduction of BP to <95th percentile.
 - b. For children with chronic renal disease, diabetes, or hypertensive target organ damage, the goal is reduction of BP to <90th percentile.
6. A “*step down*” therapy or cessation of therapy may be considered in selected patients who had uncomplicated primary hypertension which is well under control, especially overweight children who successfully lose weight. Such patients require ongoing follow-up of their BP levels and their weight status.
7. Follow-up examinations should include ongoing monitoring of BP levels, target-organ damage, periodic serum electrolyte determination in children treated with ACE inhibitors or diuretics, counseling regarding other CV risk factors, and adherence to newly adopted healthy lifestyle.

VII. TREATMENT OF SECONDARY HYPERTENSION

Treatment of secondary hypertension should be aimed at removing the cause of hypertension whenever possible.

1. Coarctation. Surgical or catheter interventional correction is indicated for coarctation of the aorta.
2. Renal parenchymal disease. The same therapy as discussed for essential hypertension is given. Salt restriction and antihypertensive

TABLE 23-6**ORAL DOSAGES OF SELECTED ANTIHYPERTENSIVE DRUGS FOR CHILDREN**

DRUGS	INITIAL DOSE	TIMES/DAY
ANGIOTENSIN-CONVERTING ENZYME INHIBITORS		
Captopril (Capoten)	0.3-0.5 mg/kg/dose (Max. 6 mg/kg/day)	3
Enalapril (Vasotec)	0.08 mg/kg/day up to 5 mg/day (Max. 0.6 mg/kg/day up to 40 mg/day) Adult: 2.5-5 mg (Max. 40 mg daily)	1-2
Lisinopril (Zestril, Prinivil)	0.07 mg/kg/day up to 5 mg/day (Max. 0.6 mg/kg/day up to 40 mg/day) Adult: 10 mg (Max. 80 mg daily)	1
ANGIOTENSIN-RECEPTOR BLOCKER		
Losartan (Cozaar)	0.7 mg/kg/day up to 50 mg/day (Max. 1.4 mg/kg/day up to 100 mg/day) Adult: 50 mg (Max. 100 mg daily)	1
CALCIUM CHANNEL BLOCKERS		
Amlodipine (Norvasc)	6-17 yr: 2.5-5 mg/day Adult: 5-10 mg (Max. 10 mg/24 hr)	1
Isradipine (DynaCirc)	0.15-0.2 mg/kg/day (Max. 0.8 mg/kg/day up to 20 mg/day)	3-4
DIURETICS		
Hydrochlorothiazide (HydroDIURIL)	1 mg/kg/day (Max. 3 mg/kg/day up to 50 mg/day) Adult: 25-100 mg	1
Chlorthalidone	0.3 mg/kg/day (Max. 2 mg/kg/day up to 50 mg/day) Adult: 12.5-25 mg	1
Furosemide (Lasix)	0.5-2 mg/kg/dose (Max. 6 mg/kg/day)	1-2
Spironolactone (Aldactone)	1 mg/kg/day (Max. 3.3 mg/kg/day up to 100 mg/day)	1-2
Triamterene (Dyrenium)	1-2 mg/kg/day (Max. 3-4 mg/kg/day up to 300 mg/day)	2
ADRENERGIC INHIBITORS		
Propranolol (Inderal)	1-2 mg/kg/day (Max. 4 mg/kg/day up to 640 mg/day)	2-3
Metoprolol (Lopressor)	1-2 mg/kg/day (Max. 6 mg/kg/day up to 200 mg/day)	2
Atenolol (Tenormin)	0.5-1 mg/kg/day (Max. 2 mg/kg/day up to 100 mg/day)	1-2
VASODILATORS, DIRECT ACTING		
Hydralazine (Apresoline)	0.75 mg/kg/day (Max. 7.5 mg/kg/day up to 200 mg/day)	4
Minoxidil (Loniten)	>12 yr: 5 mg/day (Max. 100 mg/day)	1-3

Modified from The fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents, Pediatrics 114:555-576, 2004.

drug therapy can control hypertension caused by most renal parenchymal diseases. If hypertension is difficult to control and the disease is unilateral, unilateral nephrectomy may be considered.

3. Renovascular disease may be treated by successful surgery, such as reconstruction of a stenotic renal artery or autotransplantation.
4. Hypertensions caused by tumors that secrete vasoactive substances, such as pheochromocytoma, neuroblastoma, and juxtaglomerular cell tumor, are treated primarily by surgery.

Chapter 24

Pulmonary Hypertension

I. DEFINITION

Pulmonary hypertension (PH) is present when the PA pressure is higher than the upper limit of normal, which differs according to the measurement method used.

1. In the cardiac catheterization lab, the normal PA systolic pressure in children and adults is ≤ 30 mm Hg (with the PA mean pressure ≤ 25 mm Hg) at sea level.
2. The noninvasive Doppler method, however, often overestimates the PA pressure. Using TR jet velocity and the Bernoulli equation, with an assumed RA pressure of 10 mm Hg, the upper limit of normal PA systolic pressure is around 37 mm Hg (with ranges of 36 to 40 mm Hg). The value of 37 mm Hg will result from a TR jet velocity of 2.6 m/sec in the absence of PS.

II. CAUSES

PH is a group of conditions with multiple causes rather than a single one. The causes of pulmonary hypertension can be grouped into the following five with examples of conditions listed as shown in [Box 24-1](#).

III. PATHOPHYSIOLOGY

1. The endothelial cells and lung tissues normally synthesize and/or activate some vasoactive hormones and inactivate others. Balance among the vasoactive substances maintains vascular tone in normal and pathologic situations.
 - a. Normally, balanced release of nitric oxide (NO, a vasodilator) and endothelin (a potent vasoconstrictor) by endothelial cells is a key factor in the regulation of the pulmonary vascular tone.
 - b. Prostaglandin (PG) I_2 and PGE_1 are vasodilators, whereas $PGF_{2\alpha}$ and PGA_2 are vasoconstrictors.
 - c. Stimulation of α and β -adrenoceptors produces vasoconstriction and vasodilation, respectively.
 - d. Serotonin is a vasoconstrictor that promotes smooth muscle cell hypertrophy.
 - e. Angiotensin II, a potent vasoconstrictor, is activated from angiotensin I in the lungs by angiotensin converting enzyme (ACE).
2. Reduced alveolar oxygen tension (*alveolar hypoxia*) induces vasoconstriction (by reducing NO production and increasing endothelin production).
 - a. Acidosis significantly increases PVR, acting synergistically with hypoxia.

BOX 24-1**CAUSES OF PULMONARY HYPERTENSION**

1. Large left-to-right shunt lesions (hyperkinetic pulmonary hypertension): VSD, PDA, ECD
2. Alveolar hypoxia
 - a. Pulmonary parenchymal disease
 - (1) Extensive pneumonia
 - (2) Hypoplasia of lungs (primary or secondary, such as that seen in diaphragmatic hernia)
 - (3) Bronchopulmonary dysplasia
 - (4) Interstitial lung disease (Hamman-Rich syndrome)
 - (5) Wilson-Mikity syndrome
 - b. Airway obstruction
 - (1) Upper airway obstruction (large tonsils, macroglossia, micrognathia, laryngotracheomalacia, sleep-disordered breathing)
 - (2) Lower airway obstruction (bronchial asthma, cystic fibrosis)
 - c. Inadequate ventilatory drive (central nervous system diseases, obesity hypoventilation syndrome)
 - d. Disorders of chest wall or respiratory muscles
 - (1) Kyphoscoliosis
 - (2) Weakening or paralysis of skeletal muscle
 - e. High altitude (in certain hyper-reactors)
3. Pulmonary venous hypertension: MS, cor triatriatum, TAPVR with obstruction, chronic left heart failure. Rarely, congenital pulmonary vein stenosis causes incurable pulmonary hypertension.
4. Primary pulmonary vascular disease
 - a. Persistent pulmonary hypertension of the newborn
 - b. Primary pulmonary hypertension—rare, fatal form of pulmonary hypertension with obscure cause
5. Other diseases that involve pulmonary parenchyma or pulmonary vasculature, directly or indirectly
 - a. Thromboembolism: ventriculoatrial shunt for hydrocephalus, sickle cell anemia, thrombophlebitis
 - b. Connective tissue disease: scleroderma, systemic lupus erythematosus, mixed connective tissue disease, dermatomyositis, rheumatoid arthritis
 - c. Disorders directly affecting the pulmonary vasculature: schistosomiasis, sarcoidosis, histiocytosis X
 - d. Portal hypertension (hepatopulmonary syndrome)
 - e. HIV infection

b. High altitude (with low alveolar oxygen tension) is associated with pulmonary vasoconstriction (and pulmonary hypertension), for which large species and individual variations exist.

3. Pressure (P) is related to both flow (F) and vascular resistance (R), as shown in the following formula:

$$P = F \times R$$

An increase in pulmonary blood flow, pulmonary vascular resistance, or both can result in PH. Regardless of its cause, PH eventually involves

constriction of the pulmonary arterioles, resulting in an increase in PVR and hypertrophy of the RV.

4. The normally thin RV cannot sustain sudden increase in the PA pressure over 40 to 50 mm Hg and results in RV failure. However, if PH develops slowly, the RV hypertrophies and it can tolerate much higher pressures, even suprasystemic pressures.
5. Normal pulmonary vascular resistance (PVR) is 1 Wood unit (or 67 ± 23 [SD] dyne-sec/cm²), which is about 10% of systemic vascular resistance.

IV. PATHOGENESIS OF PULMONARY HYPERTENSION

Pathogenesis differs among different subgroups of PH.

A. Hyperkinetic Pulmonary Hypertension

1. PH associated with large L-R shunt lesions (e.g., VSD, PDA) is called *hyperkinetic pulmonary hypertension*. It is the result of an increase in pulmonary blood flow, a direct transmission of the systemic pressure to the PA, and compensatory pulmonary vasoconstriction. Endothelial cell dysfunction with overproduction of endothelin and reduced NO production result.
2. Hyperkinetic PH is usually reversible if the cause is eliminated before permanent changes occur in the pulmonary arterioles (see later section). If large L-R shunt lesions are left untreated, irreversible changes take place in the pulmonary vascular bed, with severe PH and cyanosis due to a reversal of the left-to-right shunt. This stage is called Eisenmenger syndrome or pulmonary vascular obstructive disease (PVOD). Surgical correction is not possible at this stage.

B. Alveolar Hypoxia

1. An acute or chronic reduction in the oxygen tension (P_{O_2}) in the alveolar capillary region (alveolar hypoxia) elicits a strong pulmonary vasoconstrictor response, which may be augmented by acidosis. Although the exact mechanisms of the pulmonary vasoconstrictor response to alveolar hypoxia are not completely understood, endothelin and nitric oxide (NO) are the strongest candidates responsible for the response.
2. Alveolar hypoxia may be an important basic mechanism of many forms of PH, including that seen in pulmonary parenchymal disease, airway obstruction, inadequate ventilatory drive (central nervous system diseases), disorders of chest wall or respiratory muscles, and high altitude.

C. Pulmonary Venous Hypertension

1. Increased pressures in the pulmonary veins produce reflex vasoconstriction of the pulmonary arterioles and raise the PA pressure to maintain a high enough pressure gradient between the PA and

the pulmonary vein. The mechanism for the vasoconstriction is not entirely clear but a neuronal component may be present. Moreover, an elevated pulmonary venous pressure may also close small airways, resulting in alveolar hypoxia, which may contribute to the vasoconstriction. Mitral stenosis, TAPVR with obstruction (of pulmonary venous return to the LA), and chronic left-sided heart failure are examples of this entity.

2. PH with increased pulmonary venous pressure is usually reversible when the cause is eliminated.

D. Primary Pulmonary Vascular Disease

1. Primary pulmonary hypertension is characterized by progressive, irreversible vascular changes similar to those seen in Eisenmenger's syndrome but without intracardiac lesions. The pathogenesis of primary pulmonary hypertension is not fully understood, but endothelial dysfunction of the pulmonary vascular bed (with overproduction of endothelin) and enhanced platelet activities may be important factors. Overproduction of endothelin is associated with not only vasoconstriction but also cell proliferation, inflammation, medial hypertrophy, and fibrosis.
2. This condition is rare in pediatric patients; it is a condition of adulthood and is more prevalent in women. It has a poor prognosis.

E. Other Disease States

Pulmonary hypertension associated with other disease states has similar pathogenesis to that described in the above four categories, singly or in combination.

V. PATHOLOGY

1. Heath and Edwards classified the changes into six grades.
 - a. Grade 1: hypertrophy of the medial wall of the small muscular arteries
 - b. Grade 2: hyperplasia of the intima
 - c. Grade 3: hyperplasia and fibrosis of the intima with narrowing of the vascular lumen
 - d. Grades 4 to 6: dilatation and plexiform lesions, angiomatous and cavernous lesions, hyalinization of intimal fibrosis, and necrotizing arteritis
2. Changes up to grade 3 are considered reversible if the cause is eliminated. Changes seen in grades 4 through 6 are considered "irreversible" and preclude surgical repair of CHDs.
3. The progressive vascular changes that occur in primary PH are identical to those that occur with CHDs.
4. With pulmonary venous hypertension, pulmonary arteries may show severe medial hypertrophy and intimal fibrosis. However, the changes are limited to grades 1 through 3 of Heath and Edwards' classification and they are often reversible when the cause is eliminated.

VI. CLINICAL MANIFESTATIONS

1. With significant PH, exertional dyspnea and fatigue may manifest. Some patients complain of headache. Syncope, presyncope, or chest pain also occurs on exertion.
2. Cyanosis with or without clubbing may be present. The neck veins are distended and a right ventricular lift or tap occurs on palpation.
3. The S2 is loud and single. An ejection click and an early diastolic decrescendo murmur of PR are usually present along the MLSB. A holosystolic murmur of TR may be audible at the LLSB. Signs of right-sided heart failure (e.g., hepatomegaly, ankle edema) may be present.
4. The ECG shows RAD and RVH with or without “strain.” RAH is frequently seen. Arrhythmias occur in the late stage.
5. Chest radiographs show either normal or slightly enlarged heart. A prominent PA segment and dilated hilar vessels with clear lung fields are characteristic.
6. Echo studies usually demonstrate the following:
 - a. Enlargement of the RA and RV, with normal or small LV dimensions.
 - b. With an elevated RV pressure, the interventricular septum shifts toward the LV and appears flattened at the end of systole.
 - c. PA pressure can be estimated by a Doppler study (see Chapter 4 for detailed discussion).
 - (1) Using the peak TR velocity, the RV systolic pressure can be estimated by the simplified Bernoulli equation ($\Delta P = 4V^2$) and adding assumed RA pressure of 10 mm Hg. The upper limit of normal PA systolic pressure by the Doppler method is 36–40 mm Hg.
 - (2) With a shunt lesion, such as VSD or PDA, the peak systolic velocity across the shunt is used to estimate the RV pressure.
 - (3) The end-diastolic velocity of pulmonary regurgitation (PR) can be used to estimate the *diastolic* pressure in the PA. The end-diastolic (not early diastolic) velocity is measured and entered into the modified Bernoulli equation, and a normal central venous pressure of 10 mm Hg is added.
7. Natural history and prognosis
 - a. PH secondary to the upper airway obstruction is usually reversible when the cause is eliminated.
 - b. PH associated with large L-R shunt lesions or that associated with pulmonary venous hypertension improves or disappears after surgical removal of the cause, if performed early.
 - c. Chronic pulmonary conditions that produce alveolar hypoxia have a relatively poor prognosis.
 - d. Primary PH is progressive and has a fatal outcome, usually 2 to 3 years after the onset of symptoms.
 - e. PH associated with Eisenmenger syndrome, collagen disease, and chronic thromboembolism is usually irreversible and has a poor prognosis but may be stable for 2 to 3 decades.
 - f. Right-sided heart failure and cardiac arrhythmias occur in the late stage. Chest pain, hemoptysis, and syncope are ominous signs.

VII. DIAGNOSIS

1. Noninvasive tools (ECG, chest radiographs, and echo) are used to detect and estimate the severity of PH. Collectively, they are reasonably accurate in assessing severity.
2. Cardiac catheterization is performed to confirm the diagnosis and severity of PH and to determine whether the elevated pulmonary vascular resistance is due to active vasoconstriction (“responders”) or to permanent changes in the pulmonary arterioles (“nonresponders”). Protocol for vasodilator testing varies from center to center.
 - a. Nitric oxide inhalation (20 ppm) with or without increased oxygen concentration for 10 minutes is commonly used. Tolazoline (Priscoline, α -adrenoceptor blocker), intravenous prostacycline, or the administration of oxygen may also be used.
 - b. Acute “responders” should show a decrease of ≥ 10 mm Hg in the mean PA pressure with a mean PA pressure ≤ 40 mm Hg or a decrease of $\geq 20\%$ in the mean PA pressure or PVR with an unchanged or increased cardiac output.
3. Lung biopsies have been used in an attempt to evaluate the “operability” of patients with PH and CHD. Unfortunately, pulmonary vascular changes are not uniformly distributed and the biopsy findings correlated poorly with the natural history of the disease and operability. Hemodynamic data appear to predict survival better than biopsy findings.

VIII. MANAGEMENT

A. Treating Underlying Causes

Measures to remove or treat the underlying cause should be the primary emphasis whenever possible.

1. Timely corrective surgery for CHDs (such as large-shunt VSD, ECD, or PDA).
2. Tonsillectomy and adenoidectomy when the cause of PH is the upper airway obstruction.
3. Treatment of underlying diseases, such as cystic fibrosis, asthma, pneumonia, or bronchopulmonary dysplasia.

B. General Measures

General measures are aimed at preventing further elevation of PA pressure or treating its complications.

1. The patient should avoid or limit strenuous exertion, isometric activities (weight lifting), and trips to high altitude.
2. Oxygen supplementation is provided as needed.
3. The patient should avoid vasoconstrictor drugs, including decongestants with α -adrenergic properties.
4. Patients should be strongly advised to avoid pregnancy. Pregnancy may increase the risk of pulmonary embolism from deep vein thrombosis or amniotic fluid, and may cause syncope and cardiac arrest.
5. Oral contraceptives should not be used because they worsen pulmonary hypertension (surgical contraception is preferred).

6. CHF is treated with digoxin and diuretics and a low-salt diet.
7. Cardiac arrhythmias are treated with antiarrhythmic agents.
8. Partial erythropheresis is performed for polycythemia and headache.
9. Annual flu shots are recommended.

C. Anticoagulation and Antiplatelet Agents

1. Anticoagulation with warfarin (with the INR of 2.0-2.5) is widely recommended in patients with thromboembolic disease. It may be beneficial in patients with PH from other causes.
2. Some recommend antiplatelet drugs (aspirin) instead of warfarin to prevent microembolism in the pulmonary circulation.

D. Pharmacologic Treatment of Pulmonary Hypertension

The pulmonary vasodilators are used in “responders.” For nonresponders, vasodilators have limited success. Vasodilators should not be used without testing first in the catheterization laboratory.

1. **For responders.** The following vasodilators are used in responders. Most of the experiences are based on adult trials. Some vasodilators may lower the systemic vascular resistance more than the pulmonary vascular resistance and thus are not suitable.
 - a. **Nifedipine**, a calcium channel blocking agent (at a dose of 0.2 mg/kg PO q8H), is one of the oldest drugs used with beneficial effects seen in 40% of children with primary PH. Hypotension is a side effect of the medication.
 - b. **Prostacyclines.** Continuous intravenous infusion of epoprostenol (PGI_2) has been shown to improve quality of life and survival in patients with primary PH, Eisenmenger syndrome, or chronic lung disease. The starting dose of epoprostenol was 2 ng/kg/min, with increments of 2 ng/kg/min every 15 min, until desired effects appeared: the average final dose was 9 to 11 ng/kg/min.
 - c. Endothelin receptor antagonists, **bosentan** and **sitaxsenton**, have been used in both primary PH and Eisenmenger syndrome.
 - (1) In children with primary pulmonary hypertension or Eisenmenger syndrome, oral bosentan, a nonselective endothelin receptor blocker, in the dose of 31.25 mg BID for children <20 kg, 62.5 mg BID for children 20-40 kg, and 125 mg BID for children >40 kg (with or without concomitant IV prostacycline therapy) for median duration of 14 months, resulted in a significant functional improvement in about 50% of the cases. A rare side effect of the drug is increased liver enzyme.
 - (2) Sitaxsentan, a selective endothelin-A (ET_A) receptor antagonist, given orally once daily at a dose of 100 mg (for mostly adult patients and children older than 12 years), resulted in improved exercise capacity after 18 weeks of treatment. Elevation of AST and ALT was a rare side effect.

- d. Sildenafil, a phosphodiesterase inhibitor, prevents the breakdown of cyclic GMP resulting in pulmonary vasodilatation. Oral dose of 0.25 to 1 mg/kg, 4 times daily for 12 months' duration, has resulted in improvement in hemodynamics and exercise capacity. Adverse effects include headache, flushing, exacerbation of nosebleed, and rare systemic hypotension or erection.
 - e. Nitric oxide inhalation is effective in lowering PA pressure in adult respiratory distress syndrome, primary pulmonary hypertension, and persistent pulmonary hypertension of the newborn. Nitric oxide can be administered only by inhalation because it is inactivated by hemoglobin. Rebound pulmonary hypertension is problematic.
 - f. In addition to the above vasodilators, inotropic agents (e.g., digoxin, dopamine) are often helpful in lowering PA pressure.
2. **For nonresponders.** The following measures can be used in nonresponders.
- a. Nitric oxide inhalation and continuous intravenous or possibly nebulized prostacycline (prostaglandin I₂) may provide selective pulmonary vasodilatation.
 - b. Atrial septectomy (either by catheter or surgery) improves survival rates and abolishes syncope by providing a R-L atrial shunt and thereby helping to maintain cardiac output but with increased hypoxemia.
 - c. Lung or heart-lung transplantation remains the only available treatment for patients unresponsive to vasodilator treatment. Bilateral lung transplantation is preferred at most centers but some centers prefer single lung transplantation.

Chapter 25

Athletes with Cardiac Problems

Almost all states in the United States require some type of preparticipation screening of participants in organized sports. The major reason for this is to help prevent sudden unexpected death. Most physicians encounter this issue in association with high school and college sports, and therefore physicians should have a general understanding of the eligibility guidelines and the participation eligibility for patients with specific CV conditions. Athletic competitions substantially increase the sympathetic drive. The resulting increase in catecholamine levels increases BP, heart rate, and myocardial contractility and increases oxygen demand. The increase in sympathetic tone can cause arrhythmias and may aggravate existing myocardial ischemia.

I. SUDDEN CARDIAC DEATH IN YOUNG ATHLETES

A. Statistics of Sudden Unexpected Death

1. Sudden cardiac death (SCD) occurs in about 1 per 200,000 high school sports participants per academic year. It is far more common in boys than girls. In the United States, football and basketball are the sports most frequently associated with SCD.
2. The two most important groups of heart disease that cause SCD are hypertrophic cardiomyopathy (HCM) and coronary artery anomalies or diseases, accounting for nearly 70% of the cases (see [Table 25-1](#)).

B. Common Causes of SCD

1. Hypertrophic cardiomyopathy (up to 36%) and its variant (8%) account for nearly half of the unexpected SCD cases (see [Table 25-1](#)).
2. Anomalies of the coronary arteries, both congenital and acquired (atherosclerotic or the result of Kawasaki disease), is the next important group of causes of SCD, accounting for 23%.
3. Myocarditis and dilated cardiomyopathy are found in up to 8% of SCD.
4. Cardiac arrhythmias (caused by long QT syndrome, WPW syndrome, sinus node dysfunction, arrhythmogenic right ventricular dysplasia [ARVD]) account for 10% of SCD.
5. Other rare causes of SCD in athletes include severe AS or PS, Marfan syndrome (from ruptured aortic aneurysm), MVP, dilated cardiomyopathy, primary pulmonary hypertension, “commotio cordis,” sarcoidosis, and sickle cell trait.

TABLE 25-1

CARDIOVASCULAR CAUSES OF SUDDEN DEATH IN YOUNG ATHLETES (N = 690)*

CAUSE	PERCENT
Hypertrophic cardiomyopathy	36
Coronary artery anomalies, congenital and acquired	23
Possible hypertrophic cardiomyopathy	8
Myocarditis	6
Arrhythmogenic right ventricular cardiomyopathy	4
Ion channel disease	4
Mitral valve prolapse	3
Aortic rupture	3
Aortic stenosis	2
Dilated cardiomyopathy	2
Wolff-Parkinson-White syndrome	2
Others	5

Modified from Balady GJ, Ades PA: Exercise and Sports Cardiology. In Bonow O, Mann DL, Zipes DP, Libby P, eds: *Braunwald's Heart Disease*, ed 9, Saunders, Philadelphia, 2012.

*Original data from Maron BJ, Doerer JJ, Haas TS, et al: Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006, *Circulation* 119:1085-1092, 2009.

C. Preparticipation Screening

The most important reason for the screening is to detect “silent” CV disease that can cause sudden cardiac death. Detailed prospective CV screening of a large athletic population is impractical, because there are 8 to 10 million competitive athletes in the United States. Even with the use of specialized cardiologic tools, complete prevention of SCD is nearly impossible. Thus, medical clearance for sports does not necessarily imply the absence of CV disease or complete protection from sudden death.

1. Recommended screening

- The American Heart Association (AHA) has recommended 12-point screening, which has limited power to consistently identify important CV abnormalities; 8 points are related to the history and the remaining 4 are physical examination ([Box 25-1](#)).
- Although the European Society of Cardiology has recommended an ECG with each evaluation, the AHA does not recommend it. Although the ECG may detect most cases of HCM, the cost of doing ECGs versus the yield is prohibitive and the cost of evaluating false positives is too great to make this practice cost-effective.

2. Screening tools

- History and physical examination
 - Although history and physical examination can raise the suspicion of CV disease in some at-risk athletes, they do not have sufficient power to guarantee detection of many critical CV abnormalities.
 - History of syncope, chest pain, dyspnea, and fatigue, particularly when associated with exertion, is important.
 - Family history of premature cardiac death, sudden unexpected death, and heritable diseases should be noted.

BOX 25-1**THE 12 ELEMENTS: AHA RECOMMENDATIONS FOR PREPARTICIPATION CARDIOVASCULAR SCREENING OF COMPETITIVE ATHLETES****PERSONAL HISTORY***

1. Exertional chest pain/discomfort
2. Unexplained syncope or near syncope[†]
3. Excessive exertional and unexplained dyspnea/fatigue, associated with exercise
4. Prior recognition of a heart murmur
5. Elevated systolic blood pressure

FAMILY HISTORY*

6. Premature death (sudden and unexpected, or otherwise) before age 50 years due to heart disease, in ≥ 1 relative
7. Disability from heart disease in a close relative <50 years of age
8. Specific knowledge of certain cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, long QT syndrome or other ion channelopathies, Marfan syndrome, or clinically important arrhythmias

PHYSICAL EXAMINATION

9. Heart murmur[‡]
10. Femoral pulses to exclude aortic coarctation
11. Physical stigmata of Marfan syndrome
12. Brachial artery blood pressure (sitting position)[§]

*Parental verification is recommended for high school and middle school athletes.

[†]Judged not to be neurocardiogenic (vagal); of particular concern when related to exertion.

[‡]Auscultation should be performed in both supine and standing positions (or with Valsalva maneuver), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.

[§]Preferably taken in both arms.

Maron BJ et al: Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007, *Circulation* published online Mar 12, 2007.

- (c) Physical examination detects significant AS or PS or coarctation of the aorta.
 - (d) Identification of HCM by the AHA's 12 elements is unreliable because (1) most patients with HCM have the nonobstructive form of the disease (and thus, no audible heart murmur), and (2) most athletes with HCM do not experience exertional syncope or have a family history of the disease or premature sudden death.
- (2) If CV abnormalities are suspected by the AHA's screening procedure:
- (a) Specialty consultation or ordering additional testing is indicated.
 - (b) The athlete should be temporarily withdrawn from activities until the issue can be resolved.
 - (c) The utilities of an ECG and an echo study are briefly outlined in the following section, although they are not routinely recommended by the AHA.

- b. Electrocardiography. The 12-lead ECG is a practical and cost-effective strategic alternative to routine echocardiography.
- (1) The ECG is abnormal in 75% to 95% of patients with HCM. Abnormalities may include LVH, ST-T changes, and abnormally deep Q waves (owing to septal hypertrophy) with diminished or absent R waves in V5 and V6. Occasionally, “giant” negative T waves are seen in V5 and V6. Cardiac arrhythmias and first-degree AV block may be seen occasionally.
 - (2) Coronary artery abnormalities may show ST-T wave abnormalities or abnormal Q waves.
 - (3) Long QT syndrome ($QTc > 0.46$ sec), Brugada syndrome (RBBB with ST segment elevation), and other inherited syndromes can be identified by the ECG.
 - (4) The ECG may also raise suspicion of myocarditis (PVCs, ST-T changes) or arrhythmogenic RV cardiomyopathy (by T wave inversion in leads V1 through V3, tall P waves, decreased RV potentials).
 - (5) However, about 40% of trained athletes may show the following ECG abnormalities, causing confusion: (a) increased R or S wave voltages; (b) Q wave and repolarization abnormalities; and (c) Holter monitors may show frequent and/or complex ventricular tachyarrhythmias.
- c. Echocardiography. Echo study will identify HCM and other cardiac abnormalities.
- (1) In adults, HCM is diagnosed when diastolic LV wall thickness ≥ 15 mm (or on occasion, 13 or 14 mm), usually with LV dimension < 45 mm, is present. For children, z-score of 2 or more relative to BSA is theoretically compatible with the diagnosis.
 - (2) Some highly trained athletes may show LVH, making the differentiation between the physiologic hypertrophy and HCM difficult. An LV wall thickness ≥ 13 mm is very uncommon in highly trained athletes and it is always associated with an enlarged LV cavity (with LV diastolic dimension > 54 mm; ranges 55 to 63 mm). Therefore, athletes with LV wall thickness > 16 mm and a nondilated LV cavity are likely to have HCM.
 - (3) Echo will detect other CHDs (such as AS, PS), Marfan syndrome (aortic root dilatation, mitral valve prolapse), myocarditis, or dilated cardiomyopathy (LV dysfunction and/or enlargement).
 - (4) Definitive diagnosis of congenital coronary artery anomalies may not be accomplished by echo studies; it may require other tests such as CT or coronary angiography.

II. CLASSIFICATION OF SPORTS

For the purpose of making recommendations on athletes' participation eligibility, Task Force 8 of the 36th Bethesda Conference (Mitchel et al, 2005) has presented the following classification of sports (Fig. 25-1).

Figure 25-1 is useful in make sports recommendations for patients with



Increasing static component 	III. High (>50% MVC)	Bobsledding/luge*† Field events (throwing) Gymnastics*† Martial arts* Sailing Sports climbing Waterskiing*† Weight lifting*† Windsurfing*†	Bodybuilding*† Downhill skiing*† Skateboarding*† Snowboarding*† Wrestling*	Boxing*† Canoeing/kayaking Cycling*† Decathlon Rowing Speed skating*† Triathlon*†
	II. Moderate (20%-50% MVC)	Archery Auto racing*† Diving*† Equestrian*† Motorcycling*†	Football (American)* Field events (jumping) Figure skating* Rodeoing*† Rugby Running (sprint) Surfing*† Synchronized swimming†	Basketball* Ice hockey* Cross-country skiing (skating technique) Lacrosse* Running (middle distance) Swimming Team handball
	I. Low (<20% MVC)	Billiards Bowling Cricket Curling Golf Rifiery	Baseball/softball* Fencing Table tennis Volleyball	Badminton Cross-country skiing (classic technique) Field hockey* Orienteering Race walking Racquetball/squash Running (long distance) Soccer* Tennis
Increasing dynamic component 				
A. Low ($<40\%$ max O_2) B. Moderate ($40\%-70\%$ max O_2) C. High ($>70\%$ max O_2)				

FIGURE 25-1

Classification of sports. Max O_2 , maximal oxygen uptake; MVC, maximal voluntary contraction; *Danger of bodily collision, †Increased risk if syncope occurs. (Modified from Mitchel JH, Haskell W, Snell P, et al., Task Force 8: Classification of sports, *J Am Coll Cardiol* 45:1364-1367, 2005.)

heart problems. Sports are divided into two broad types, dynamic and static, and each sport is categorized by the level of intensity (low, medium, high). Most sports activities are a combination of static and dynamic exercises.

A. Dynamic (Isotonic) Exercise

1. Dynamic exercise involves changes in muscle length and joint movement with rhythmic contractions that develop relatively small intramuscular force.
2. It causes a marked increase in oxygen consumption with a substantial increase in cardiac output, heart rate, and stroke volume. It increases systolic pressure but decreases diastolic pressure and systemic vascular resistance. It primarily causes a volume load on the left ventricle.

B. Static Exercise

1. Static (isometric) exercise involves development of relatively large intramuscular force with little or no change in muscle length or joint movement.
2. It causes a small increase in oxygen consumption, cardiac output, and heart rate and no change in stroke volume. There is a marked increase in systolic, diastolic, and mean arterial pressures and no appreciable change in total peripheral resistance. Static exercise causes a pressure load on the LV.

III. ELIGIBILITY DETERMINATION OF ATHLETES WITH CARDIOVASCULAR DISEASES

Most of the following recommendations are excerpts from the 36th Bethesda Conference (Maron et al, 2005). These recommendations apply to athletes in high school and college. For further details on a specific condition, the readers are encouraged to refer to the original articles.

A. Acyanotic Congenital Heart Defects

1. **L-R shunt lesions.** Participation eligibility of athletes with L-R shunt lesions is primarily determined by the level of pulmonary artery (PA) systolic pressure and the status of left ventricular (LV) systolic function.
 - a. Pulmonary artery systolic pressure (PA SP):
 - (1) When PA SP is ≤ 30 mm Hg in the cardiac catheterization lab (or Doppler-estimated PA systolic pressure < 36 to 40 mm Hg), full participation in all competitive sports is allowed.
 - (2) When PA SP is > 30 mm Hg (or Doppler-estimated PA systolic pressure > 36 to 40 mm Hg), some limitations apply. With mild pulmonary hypertension (PH), low-intensity sports (class IA) are permitted. With severe PH or PVOD, no competitive sports are allowed.
 - b. Left ventricular (LV) systolic function:
 - (1) When LV ejection fraction (EF) is $\geq 50\%$, full participation is allowed.
 - (2) With LV EF 40% to 50% , low-intensity static sports (class IA, IB, and IC) are allowed.
 - (3) With LV EF $< 40\%$, no competitive sports are allowed.
2. **Obstructive lesions**
 - a. For mild PS (Doppler gradient < 30 mm Hg) or mild AS (peak Doppler gradient < 40 mm Hg) and mild COA, all competitive sports are allowed.
 - b. With moderate PS (Doppler gradient 40 - 60 mm Hg) or moderate AS (Doppler gradient 40 - 70 mm Hg), classes IA, IB, and possibly IIA are allowed.
 - c. Following correction of more severe abnormalities to mild abnormality, appropriate level of sports may be allowed 4 weeks after balloon procedures or 3 months after surgery.

B. Cyanotic Congenital Heart Defects

In patients with arterial oxygen desaturation from cyanotic CHD, moderate to severe restriction in sports participation is recommended.

1. Patients with cyanotic CHDs, which are unoperated or for which palliative procedures have been done, can only participate in low-intensity competitive sports, such as class IA.
2. Most patients with cyanotic CHD for which surgical repair has been done can only participate in low-intensity sports.
3. Patients who have received an excellent result from the surgical repair of TOF or arterial switch operation for TGA may participate in all competitive sports.

C. Coronary Artery Abnormalities

1. For most patients with congenital abnormalities of the coronary arteries or following Kawasaki disease, moderate to severe restriction in sports participation is recommended.
2. Those children who had no coronary artery involvement during the acute phase of Kawasaki disease may participate in all sports 6 to 8 weeks after the illness. Stress testing is often required before prescribing participation eligibility.

D. Valvular Heart Diseases

The severity of the valvular lesion determines eligibility for participation in competitive sports.

1. In patients with mild valvular lesions (such as MS, MR, AS, and AR), participation in all competitive sports is allowed.
2. In patients with moderate valvular lesions, participation is limited to low- to moderate-intensity sports.
3. In patients with severe obstructive lesions such as AS, participation in competitive sports is not permitted.
4. In patients with valvular lesions that produce significant pulmonary hypertension, no participation in competitive sports is permitted.
5. For those patients with prosthetic valves and taking warfarin, no sports involving the risk of bodily contact are allowed.

E. Cardiomyopathy, Pericarditis, and Other Myocardial Diseases

1. Athletes who have either confirmed or probable diagnosis of HCM or arrhythmogenic RV dysplasia are excluded from most competitive sports, with the possible exception of class IA sports.
2. Athletes with myocarditis or pericarditis of any etiology should be excluded from all competitive sports during the acute phase. After complete recovery from these illnesses, they may gradually participate in sports.
3. Athletes with Marfan syndrome can participate only in class IA or IB sports
4. Athletes with MVP who have any symptoms or abnormalities in ECG, LV function, or arrhythmias are permitted to participate only in low-intensity sports.

F. Cardiac Arrhythmias, AV Block, and Intraventricular Blocks

The presence of a symptomatic cardiac arrhythmia requires exclusion from physical activity until this problem can be adequately evaluated and controlled by a cardiologist.

1. Atrial arrhythmias
 - a. Patients with premature atrial contractions (PACs) can participate in all competitive sports.
 - b. Asymptomatic athletes with atrial flutter or fibrillation and a structurally normal heart may participate in competitive sports when the arrhythmias are fully under control either by medication or ablation.

- c. Athletes with SVT and a structurally normal heart may participate in all competitive sports when the SVT is in full control with medication or following successful ablation.
 - d. Asymptomatic adult athletes with WPW preexcitation with no history of SVT may participate in all competitive sports, but children with the same diagnosis require in-depth evaluation.
2. Ventricular arrhythmias
- a. For athletes with a structurally normal heart who have PVCs or more complex arrhythmias, an exercise stress test is a useful technique. If the PVCs disappear when the heart rate reaches 140 to 150 beats per minute, the PVCs are benign and full participation may be permitted.
 - b. Athletes with ventricular tachycardia (VT) who had successful treatment to prevent recurrence of the arrhythmias may participate in sports, provided that VT is not inducible by exercise stress test or electrophysiologic study.
 - c. Athletes with long QT syndrome can participate only in class IA sports.
 - d. Athletes who had a successful ablation for any of the arrhythmias may participate in all competitive sports after verification of the success by appropriate tests.
3. Atrioventricular or intraventricular blocks
- a. Athletes with first-degree atrioventricular (AV) block or Mobitz type 1 second-degree AV block can participate in all sports provided the block does not worsen with exercise.
 - b. Athletes with a Mobitz type 2 second-degree AV block or complete heart block usually require pacemaker implantation before being permitted to participate in any sports.
 - c. Asymptomatic athletes with RBBB or LBBB who do not have ventricular arrhythmias or develop AV block during exercise can participate in all sports.
 - d. Patients with LBBB who have an abnormal prolongation of HV interval on electrophysiologic study should receive a pacemaker.
4. Cardiac pacemakers and anticoagulation. Athletes who have a pacemaker implanted and those who are on anticoagulation should not be permitted to engage in activities with danger of bodily collision. Participation in class IA sports is usually permitted.

IV. ATHLETES WITH SYSTEMIC HYPERTENSION

A. Blood Pressure and Type of Exercise

Changes in blood pressure depend on the type of exercise athletes are engaged in.

- 1. Dynamic exercise causes a substantial increase in systolic pressure, heart rate, stroke volume, and cardiac output. A moderate increase in mean arterial pressure and a decrease in diastolic pressure occur, with a marked decrease in total peripheral resistance.
- 2. Static exercise, in contrast, causes a small increase in cardiac output and heart rate and no change in stroke volume. There is a marked

increase in systolic, diastolic, and mean arterial pressures and no appreciable change in total peripheral resistance.

B. Recommendations of Task Force 5: 36th Bethesda Conference (Kaplan et al, 2005)

1. Athletes with prehypertension:
 - a. They may participate in physical activity, but should be encouraged to modify lifestyle (such as weight control).
 - b. If prehypertension persists, echo studies are done to see if there is LVH (beyond that seen with “athletes’ heart”).
 - c. If LVH is present, athletic participation is limited until BP is normalized by appropriate drug therapy.
2. Athletes with stage 1 hypertension:
 - a. They may participate in any competitive sports, in the absence of target organ damage, including LVH or concomitant heart disease. However, hypertension should be checked every 2-4 months (or more frequently) to monitor the impact of exercise.
 - b. If LVH is present, athletic participation is limited until BP is normalized by appropriate drug therapy.
3. Athletes with stage 2 (severe) hypertension: Even in the absence of target-organ damage (such as LVH), athletic participation should be restricted, particularly from high static sports (class IIIA, IIIB, and IIIC), until their hypertension is controlled by either lifestyle modification or drug therapy.

C. Drug Treatment

1. All drugs being taken must be registered with appropriate governing bodies to obtain a therapeutic exemption. When hypertension coexists with another cardiovascular disease, eligibility for participation in competitive sports is usually based on the type and severity of the associated condition.
2. With respect to the treatment of hypertension, β -blockers are not banned for most sports, including football and basketball, but they are not good choices because they reduced the athletes’ maximum performance.
3. ACE inhibitors and calcium channel blockers are preferred to β -adrenergic blockers. However, one should be aware of potential teratogenic effects of ACE inhibitors if taken during pregnancy.
4. It should be noted that β -blockers that are used to treat hypertension and arrhythmias are expressly banned in sports such as riflery (Class IA) and archery (class IIA) in which the athlete would benefit from a slow heart rate. Therefore, β -blockers should not be prescribed for athletes in these sports because it would risk them having a positive drug test.

High levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and low levels of high-density lipoprotein cholesterol (HDL-C) are all risk factors for coronary atherosclerosis. A link has been established between increased levels of triglycerides (TG) and coronary heart disease as well. Cholesterol reduction results in reduced angiographic progression of coronary artery disease and even modest regression in some cases. Therefore, controlling dyslipidemia has become a primary goal of reducing premature coronary artery disease (CAD). It has been established that the coronary arteriosclerosis begins to develop during childhood. In 2011, the Expert Panel convened by the National Heart Lung and Blood Institute (NHLBI) made recommendations on screening for dyslipidemia in children in an effort to reduce the prevalence of premature CAD.

I. DIAGNOSIS OF DYSLIPIDEMIA

Diagnosis of dyslipidemia is made by measuring blood lipid, lipoproteins, or apolipoprotein factors.

1. The routine lipid profile typically includes: total cholesterol (TC), HDL-C, LDL-C, and triglycerides (TG). A lipoprotein analysis is obtained after an overnight fast of 12 hours. The LDL level is usually estimated by the Friedewald formula:

$$\text{LDL} = \text{Total cholesterol} - \text{HDL} - (\text{Triglyceride}/5)$$

This formula is not accurate if the child is not fasting, if the triglyceride level is >400 mg/dL, or if chylomicrons or dysbetalipoproteinemia (type III hyperlipoproteinemia) is present. Methods are currently available to measure LDL-C directly, which does not require a fasting specimen.

2. An extended profile may also include very-low-density lipoprotein cholesterol (VLDL-C), non-HDL cholesterol (non-HDL-C), and the ratio of total cholesterol to HDL-C.
3. Non-HDL cholesterol (non-HDL-C): Serum non-HDL cholesterol (total cholesterol minus HDL cholesterol) is considered a better screening tool than LDL cholesterol for the assessment of CAD risk because it includes all classes of atherogenic (apolipoprotein B-containing) lipoproteins: VLDL-C, intermediate density lipoproteins (IDL), LDL-C, and lipoprotein (a) or Lp(a). Non-HDL-C from a nonfasting lipid profile is recommended in routine lipid screening.
4. The ratio of the total cholesterol (TC) to HDL cholesterol (TC-to-HDL-C ratio) is a useful parameter for assessing risk for cardiovascular (CV) disease. The usual TC-to-HDL-C ratio in children is approximately 3 (based on

TC of 150 mg/dL and an HDL-C of 50 mg/dL). The higher the ratio, the higher is the risk of developing CV disease.

5. Small, dense LDL particles: In recent years, small, dense LDL particles have been shown to be more important than the total LDL levels in coronary artery disease. The size of LDL particles is not routinely measured because the presence of this phenotype is predictable. It occurs in association with elevated triglyceride levels (>140 mg/dL) and a decreased HDL-C level (<40 mg/dL in men; <50 mg/dL in women). Although not routinely measured, small, dense LDL can be measured directly by commercial laboratories.

II. NORMAL LEVELS OF LIPIDS AND LIPOPROTEINS

Table 26-1 shows normal, borderline, and abnormal levels of lipid and lipoprotein levels in children. Table 26-2 shows those values for young adults. In children, TC \geq 200 mg/dL; LDL-C \geq 130 mg/dL; TG \geq 100 mg/dL for <10 yr and \geq 1300 mg/dL for 10-19 yr; and HDL-C <40 mg/dL are considered abnormal.

TABLE 26-1
CONCENTRATIONS OF PLASMA LIPID, LIPOPROTEIN, AND APOLIPOPROTEIN IN CHILDREN AND ADOLESCENTS (MG/DL): LOW, ACCEPTABLE, BORDERLINE, AND HIGH

CATEGORY	LOW	ACCEPTABLE	BORDERLINE	HIGH
Total cholesterol	-	<170	170-199	\geq 200
LDL cholesterol	-	<110	110-129	\geq 130
Non-HDL cholesterol	-	<120	120-144	\geq 145
Triglycerides: 0-9 years	-	<75	75-99	\geq 100
10-19 years	-	<90	90-129	\geq 130
HDL cholesterol	<40	>45	40-45	-
Apolipoprotein A-1	<115	>120	115-120	-
Apolipoprotein B		<90	90-109	\geq 110

From Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report, Pediatrics 128:S213-S256, 2011.

TABLE 26-2
RECOMMENDED CUT POINTS FOR LIPID AND LIPOPROTEIN LEVELS IN YOUNG ADULTS (MG/DL)

CATEGORY	LOW	BORDERLINE-LOW	ACCEPTABLE	BORDERLINE-HIGH	HIGH
Total cholesterol	-	-	<190	190-224	\geq 225
LDL cholesterol	-	-	<120	120-159	\geq 160
Non-HDL cholesterol	-	-	<150	150-189	\geq 190
Triglycerides	-	-	<115	115-149	\geq 150
HDL cholesterol	<40	40-44	>45	-	-

From Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report, Pediatrics 128:S213-S256, 2011.

III. CLASSIFICATION OF DYSLIPIDEMIAS

A. Secondary Dyslipidemia

Secondary dyslipidemia is caused by associated diseases or conditions and is much more common than primary dyslipidemia. The majority of cases found during screening will be secondary forms. Evidence of accelerated atherosclerosis from secondary causes of dyslipidemia is as impressive as that of primary causes.

1. Each child with dyslipidemia should have laboratory tests to help rule out secondary causes of dyslipidemia. The tests should include (a) fasting blood glucose, (b) renal function, (c) liver function, and (d) thyroid function.
2. **Box 26-1** lists causes of secondary dyslipidemia. The most common cause of pediatric dyslipidemia is obesity. Medications such as oral contraceptives, isotretinoin (Accutane), anabolic steroids, diuretics, β -blockers, and estrogens are uncommon causes of dyslipidemia. Medical conditions including hypothyroidism, renal failure, nephrotic syndrome, and alcohol usage are less common causes of secondary dyslipidemia.
3. Most secondary causes of dyslipidemia raise triglycerides (TG) and often lower HDL-C levels, with the exception of (a) increased levels of HDL-C seen with estrogen and (b) increased LDL-C seen with nephrosis, systemic lupus, primary biliary cirrhosis, protease inhibitors (for treatment of HIV), and hypothyroidism.
4. When the diagnosis of secondary dyslipidemia is made, one should treat the associated disorder producing the dyslipidemia first, such as diabetes, obesity, or nephritic syndrome, and then treat the dyslipidemia using the same guidelines as in primary dyslipidemia.

BOX 26-1

CAUSES OF SECONDARY DYSLIPIDEMIA

Metabolic	Metabolic syndrome, diabetes, lipodystrophies, glycogen storage disorders
Renal Disease	Chronic renal failure, nephrotic syndrome, glomerulonephritis, hemolytic uremic syndrome
Hepatic	Biliary atresia, cirrhosis
Hormonal	Estrogen, progesterone, growth hormone, hypothyroidism, corticosteroids
Lifestyle	Obesity, physical inactivity, diets rich in fat and saturated fat, alcohol intake
Medications	Isotretinoin (Accutane), certain oral contraceptives, anabolic steroids, thiazide diuretics, β -adrenergic blockers, anticonvulsants, glucocorticoids, estrogen, testosterone, immunosuppressive agents (cyclosporine), antiviral agents (HIV protease inhibitor)
Others	Kawasaki disease, anorexia nervosa, post-solid organ transplantation, childhood cancer survivor, progeria, idiopathic hypercalcemia, Klinefelter syndrome, Werner syndrome

B. Selected Primary Dyslipidemias

Primary dyslipidemias are far less commonly found in the screening process. Five well-known primary dyslipidemias are presented in summary format in Table 26-3.

TABLE 26-3

SELECTED PRIMARY DYSLIPIDEMIAS

LIPOID DISORDERS	CLINICAL INFORMATION
Familial Hypercholesterolemia (FH): FH Heterozygotes	Fairly common (1 in 500 people) One out of 2 siblings and one parent have \uparrow TC (>240 mg/dL; Avg, 300 mg/dL) and \uparrow LDL (>160 mg/dL; Avg, 240 mg/dL). Unaffected are perfectly normal. Xanthomas (of Achilles tendon or extensor tendons of hands) in parents (seen in 10% to 15%) almost confirm the diagnosis. TX: (a) Diet low in fat and cholesterol and high in fiber. (b) Statins are the drugs of choice.
FH Homozygotes	One in a million children TC and LDL-C are 5 to 6 times higher than normal. (TC average levels 700 mg/dL and may reach ≥ 1000 mg/dL). Planar xanthomas may be present by age 5 yr (flat, orange-colored lesions in the webbing of the hands and over the elbows and buttocks). Tendon xanthomas, arcus corneae, and significant CAD are often present by age 10 years. Atherosclerosis often results in aortic stenosis. TX: (a) High-dose statins and niacin. (b) Will require LDL apheresis (with extracorporeal affinity LDL absorption column and plasma reinfusion) every 2 weeks.
Familial Combined Hyperlipidemia (FCH)	AD disorder (3 times more frequently than FH) Characterized by variable lipid phenotypic expression: \uparrow LDL alone, \uparrow LDL + \uparrow TG, or normal LDL with \uparrow TG (difficult to separate it from FH). TC (190-220 mg/dL) and LDL (normal or mildly \uparrow) are lower than in patients with FH. Diagnosis suspected when a parent or sibling has a different lipoprotein phenotype than the proband. LDL levels fluctuate from time to time, with TG levels fluctuating in the opposite direction. Usually no tendon xanthomas are present. Often other signs of the metabolic syndrome (e.g., visceral obesity, hyperinsulinemia, glucose intolerance, and hypertension) are present. TX: (a) Low fat and low cholesterol diet, (b) low glycemic index foods, and (c) weight control + exercise. (d) Statins are the most effective drugs in lowering LDL. (e) Drug therapy if TG (>350 mg/dL) to prevent pancreatitis. (f) Metformin (\pm)
Familial Hypertriglyceridemia	AD disorder, caused by lipoprotein lipase (LPL) deficiency, resulting in hepatic overproduction of VLDL-C. TG typically increased (200-1000 mg/dL) but TC is not increased. High TG levels accompany (a) \downarrow HDL, (b) the production of smaller, denser LDL particles (more atherogenic), and (c) a hypercoagulable state. TX: (a) Diet very low in fat and simple sugar; (b) lifestyle change with exercise; (c) when TG reaches 500-1000 mg/dL, pancreatitis is a major concern (fibrate or niacin may be used).

TABLE 26-3

SELECTED PRIMARY DYSLIPIDEMIAS (Continued)

LIPID DISORDERS	CLINICAL INFORMATION
Dysbetalipoproteinemia (Type III Hyperlipoproteinemia)	Rare AR disorder, due to a defect in apo E, resulting in increased accumulation of chylomicron remnants and VLDL remnants. Both TC and TG increased equally to >300 mg/dL (not usually seen in childhood). (TC: 250-500 mg/dL; TG: 50-600 mg/dL) TX: (a) Low fat and low glycemic index diet; (b) fibric acid or statin is very effective.
Familial Hypoalphalipoproteinemia (Low HDL Syndrome)	AD disorder, caused by decreased concentration of apoA-I and apoA-II and absent apoC-III. Low HDL-C increases the risk of premature CAD. <i>Tangiers disease</i> : HDL nearly absent (with markedly enlarged yellow tonsils). TX: (a) Low carbohydrate and low fat diet. (b) Exercise and weight loss are also helpful. (c) Goal is to keep LDL low.

AD, autosomal dominant; AR, autosomal recessive; Avg, average; CAD, coronary artery disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein; TC, total cholesterol; TG, triglycerides; TX, treatment.

IV. LIPID SCREENING

In 2011 the Expert Panel convened by the National Heart Lung and Blood Institute (NHLBI) made the following recommendations. These recommendations are major changes from the past recommendations of *selective* screening of children and adolescents with family history of premature CV disease or those with at least one parent with high serum cholesterol levels (by the Expert Panel of 1991).

The new recommendations are as follows.

- Universal screening** is recommended for children 9-11 years old and patients 17-21 years old (see Box 26-2).
 - For universal screening, either nonfasting lipid profile (non-FLP) or fasting lipid panel (FLP) is acceptable.
 - Non-HDL-cholesterol = Total cholesterol – HDL cholesterol.
 - Non-HDL-C has been shown to be as powerful a predictor of atherosclerosis as any other lipoprotein cholesterol measurement in children and adolescents.
 - If non-HDL-C is abnormal (≥ 145 mg/dL), the average of two fasting lipid profiles is obtained to get LDL-C and triglycerides (TG).
- Selective screening** is recommended for children in other age groups (i.e., ages 2-8 yrs and ages 12-16 yrs) if any of the following applies (see Box 26-2). Measure FLP twice and average the results.
 - Positive family history (see Box 26-3 for details)
 - Parent(s) with total cholesterol (TC) ≥ 240 mg/dL or known dyslipidemia
 - Child who has moderate- to high-level **risk factors** such as diabetes, hypertension, BMI ≥ 85 th percentile, or smokes cigarettes (see Box 26-3).
 - Child who has a moderate- or high-risk **medical condition** (such as diabetes, chronic renal disease, posttransplant patients, Kawasaki disease, HIV infection, nephritic syndrome, and others) (see Box 26-3).

BOX 26-2**RECOMMENDATIONS FOR LIPID ASSESSMENT ACCORDING TO AGE GROUP****AGE GROUP**

<2 years	No lipid screening
2 to 8 years	<p>Selective screening. Measure FLP twice and average the result if any of the following applies:</p> <ul style="list-style-type: none"> • Positive family history (see below) • Parent with TC ≥ 240 mg/dL or known dyslipidemia • Child has diabetes, hypertension, BMI ≥ 95th%, or smokes cigarettes • Child has a moderate- or high-risk medical condition (see Box 26-3) <p>Interpret the results according to Table 26-1.</p>
9 to 11 years	<p>Universal screening (by either non-FLP or FLP)</p> <p>Non-FLP: Calculate non-HDL cholesterol (non-HDL cholesterol = TC – HDL cholesterol).</p> <p>If non-HDL cholesterol ≥ 145 mg/dL or \pm HDL < 40 mg/dL, measure FLP twice and average results.</p> <p>OR</p> <p>FLP:</p> <p>If LDL cholesterol ≥ 130 mg/dL; \pm non-HDL cholesterol ≥ 145 mg/dL; \pm HDL cholesterol < 40 mg/dL; \pm triglycerides ≥ 100 mg/dL if < 10 yr; or ≥ 130 mg/dL if ≥ 10 yr, repeat FLP and average results.</p> <p>Interpret the results according to Table 26-1.</p>
12 to 16 years	<p>Selective screening</p> <p>Measure FLP twice and average results if any of the following applies:</p> <ul style="list-style-type: none"> • Positive family history (see Box 26-3) • Parent with TC ≥ 240 mg/dL or known dyslipidemia • Child has diabetes, hypertension, BMI ≥ 85th percentile, or smokes cigarettes • Child has a moderate- or high-risk medical condition (see following) <p>Interpret the results according to Table 26-1.</p>
17 to 21 years	<p>Universal screening once in this time period (by either non-FLP or FLP)</p> <p><i>For 17-19 yr:</i></p> <p>Non-FLP: Calculate non-HDL-cholesterol.</p> <p>If non-HDL cholesterol ≥ 145 mg/dL or \pm HDL < 40 mg/dL, measure FLP twice and average results.</p> <p>OR</p> <p>FLP:</p> <p>If LDL cholesterol ≥ 130 mg/dL; \pm non-HDL-cholesterol ≥ 145 mg/dL; \pm HDL cholesterol < 40 mg/dL or \pm triglycerides ≥ 130 mg/dL, repeat FLP and average results.</p> <p>Interpret the results according to Table 26-1.</p>

BOX 26-2**RECOMMENDATIONS FOR LIPID ASSESSMENT ACCORDING TO AGE GROUP (Continued)***For 20-21 yr:*

Non-FLP: Calculate non-HDL cholesterol

If non-HDL cholesterol ≥ 190 mg/dL or \pm HDL cholesterol < 40 mg/dL, measure FLP twice and average results.

OR

FLP:

If LDL cholesterol ≥ 160 mg/dL; \pm non-HDL cholesterol ≥ 190 mg/dL; \pm HDL cholesterol < 40 mg/dL or \pm triglycerides ≥ 150 mg/dL, repeat FLP and average results.Interpret the results according to [Table 26-1](#) or [Table 26-2](#).

BMI, body mass index; Non-FLP, non-fasting lipid profile; FLP, fasting lipid panel; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol.

From Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report, Pediatrics 128:S213-S256, 2011.

BOX 26-3**CARDIOVASCULAR RISK FACTOR CATEGORIES****POSITIVE FAMILY HISTORY**

Parent, grandparent, aunt/uncle, or sibling with myocardial infarction, angina, coronary artery bypass graft/stent/angioplasty, or sudden cardiac death, at < 55 yr for males; < 65 yr for females.

RISK FACTORS

High-level risk factors:

- Hypertension that requires drug therapy (BP ≥ 99 th percentile + 5 mm Hg)
- Current cigarette smoker
- BMI ≥ 97 th percentile
- Presence of high-risk conditions, including diabetes mellitus (see following)

Moderate-level risk factors:

- Hypertension that does not require drug therapy
- BMI at the ≥ 95 th percentile, < 97 th percentile
- HDL cholesterol < 40 mg/dL
- Presence of moderate-risk conditions (see following)

SPECIAL RISK CONDITIONS

High-risk conditions:

- Type-1 and type-2 diabetes mellitus
- Chronic kidney disease/end-stage renal disease/postrenal transplant
- Postorthotopic heart transplant
- Kawasaki disease with current aneurysm

Moderate-risk conditions:

- Kawasaki disease with regressed coronary aneurysm
- Chronic inflammatory disease (systemic lupus erythematosus, juvenile rheumatoid arthritis)
- HIV infection
- Nephrotic syndrome

BMI, body mass index; HDL, high-density lipoprotein.

From Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report, Pediatrics 128:S213-S256, 2011.

V. WHAT TO DO WITH THE RESULTS OF SCREENING

1. If non-HDL-C is ≥ 145 mg/dL in non-FLP, the averages of two FLPs are obtained to get LDL-C and TG levels. The following are abnormal levels (by FLPs):
 - LDL-cholesterol > 130 mg/dL
 - Triglycerides (TG) > 100 mg/dL for children < 10 years
 - Triglycerides (TG) > 130 mg/dL for 10-19 years
2. When lipid profiles are abnormal, obtain other laboratory tests to rule out secondary dyslipidemia: fasting blood glucose, renal function, liver function, and thyroid function tests.
3. For children with high LDL-C levels:
 - a. Initial dietary management and lifestyle changes are used with the Cardiovascular Health Integrated Lifestyle Diet-1 (CHILD-1) and CHILD-2-LDL (see Table 26-4 for CHILD diets).
 - b. Lipid-lowering drugs ("statins") are considered if the diets are unsuccessful in lowering LDL-C. Indications and dosages of the statins follow.
4. For children with high TG levels:
 - a. Dietary therapy and lifestyle changes are used as the primary tools, with CHILD-1 for 3 to 6 months advancing to CHILD-2-TG.
 - b. Weight control efforts, reduction of sugar consumption, and increased consumption of fish (or omega-3 fish oil) are used.
 - c. Drugs are not recommended to reduce TG. Further discussion follows in this chapter.
5. Those children with LDL-C ≥ 250 mg/dL and those with TG ≥ 500 mg/dL should be referred to lipid specialists.

TABLE 26-4

NUTRIENT COMPOSITION OF CHILD DIETS

NUTRIENTS (% TOTAL CALORIES)	CHILD-1	CHILD-2-LDL	CHILD-2-TG
Total fat	$< 30\%$	25% to 30%	25% to 30%
Saturated fat	7% to 10%	$\leq 7\%$	$\leq 7\%$
Cholesterol	300 mg/day	< 200 mg/day	< 200 mg/day
Mono- and poly-unsaturated fatty acids	20%	$\approx 10\%$	$\approx 10\%$
Carbohydrate	50% to 55%		
Protein	15% to 20%		
Others	Reduce <i>trans</i> fat intake May add plant sterol or plant sterol esters, or water-soluble fiber psyllium	Avoid <i>trans</i> fat as much as possible	Decrease sugar intake Increase intake of com- plex carbohydrate Increase dietary fish (omega 3-fatty acids)

CHILD, Cardiovascular Health Integrated Lifestyle Diet; LDL, low-density lipoprotein; TG, triglycerides.

VI. MANAGEMENT OF HYPERCHOLESTEROLEMIA

A. Dietary Management

1. Reduced intake of saturated fat and cholesterol is most basic to the dietary therapy of hypercholesterolemia. Diet therapy is prescribed in two steps that progressively reduce the intake of saturated fats and cholesterol.
 - a. The CHILD-1 diet for 3-6 months is the first stage in dietary change (Table 26-4).
 - b. If this diet fails to lower LDL-C levels to ≤ 130 mg/dL in 6 months, a more stringent diet, CHILD-2-LDL, is used for an additional 6 months.
2. If the dietary intervention with CHILD-2-LDL fails, one may proceed with drug therapy (see following).

B. Drug Therapy

1. Lipid-lowering drugs
 - a. Five well-known classes of lipid-lowering drugs have been used for adults with dyslipidemia. They are (1) bile acid sequestrants, (2) HMG-CoA reductase inhibitors (statins), (3) cholesterol absorption inhibitors, (4) nicotinic acid (niacin, vitamin B3), and (5) fibric acid derivatives. The mechanisms of action, side effects, and ranges of adult dosages of the lipid-lowering agents are presented in Table 26-5.
 - b. The bile acid sequestrants (cholestyramine, colestipol) are not used widely because they suffer from a low compliance rate (due to gritty texture and gastrointestinal complaints) and they provide only a modest reduction of LDL cholesterol level. Ezetimibe, a cholesterol absorption inhibitor, is effective in lowering blood cholesterol levels, but pediatric experience is quite limited. Nicotinic acid and fibrates have been shown to lower LDL-C and TG levels and increase HDL-C levels in adults, but they are not frequently used in adolescents because of limited data available.
2. The statins
 - a. The statins (HMG-CoA reductase inhibitors) are the most effective drugs in lowering LDL-C in adults as well as in children and adolescents. The statins inhibit the 3-hydroxy-3-methylglutaryl coenzyme A-reductase (HMG-CoA reductase), which is the rate limiting step in the endogenous production of cholesterol in the hepatic cells.
 - b. Indications for the use of statins:
 - (1) Decision to use statins depends not only on the LDL-C levels (>130 mg/dL) but also in the presence of risk factors, such as positive family history, high-level risk factors, or risk conditions. The indications for consideration of drug therapy are detailed in Box 26-4.
 - (2) Statin therapy is NOT indicated for children with LDL cholesterol 130-189 mg/dL in a child ≥ 10 years in the absence of a positive family history and high- or moderate-level risk factor or risk (as outlined in Box 26-3). They should continue with lifestyle changes (CHILD-2-LDL), plus weight management if the BMI is at the ≥ 85 th percentile.

TABLE 26-5

SUMMARY OF LIPID-LOWERING DRUGS

DAILY DOSAGE RANGE	MECHANISM OF ACTION	SIDE EFFECTS	DAILY DOSAGE RANGE
Bile Acid Sequestrants: Cholestyramine (Questran), Colestipol (Colestid), Colesevelam (WelChol)	Increases excretion of bile acids in stool; increases LDL receptor activity	Constipation, nausea, bloating, flatulence, transient increase in transaminase and alkaline phosphatase levels, increased triglyceride levels (\pm), possible prevention of absorption of fat-soluble vitamins	Related to levels of cholesterol, not body weight
HMG-CoA Reductase Inhibitors (Statins): Atorvastatin (Lipitor), Fluvastatin (Lescol), Lovastatin (Mevacor), Pravastatin (Pravachol), Rosuvastatin (Crestor), Simvastatin (Zocor)	Inhibits HMG-CoA reductase, with resulting decrease in cholesterol synthesis; increases LDL receptor activity; and reduces LDL and VLDL secretion by the liver	Mild gastrointestinal symptoms, myositis syndrome, elevated hepatic transaminase levels, increased CPK levels Contraindicated during pregnancy because of potential risk to a developing fetus Risk of myopathy is higher with a high dose of simvastatin (80 mg) and is lower with atorvastatin or rosuvastatin	Adult dose ranges: Atorvastatin: 10-80 mg Fluvastatin: 20-80 mg Lovastatin: 20-80 mg Pravastatin: 10-40 mg Simvastatin: 10-40 mg The starting dose for children: Atorvastatin: 10 mg Fluvastatin: 20 mg Lovastatin: 10 mg Pravastatin: 10 mg Simvastatin: 10 mg
Cholesterol Absorption Inhibitors: Ezetimibe (Zetia; Ezetrol)	Selective inhibition of intestinal sterol absorption	Abdominal pain, rhabdomyolysis (\pm)	Adults: 10 mg/day
Nicotinic Acid (Niacin, Vitamin B₃)	Decreases plasma levels of free fatty acid; possibly inhibits cholesterol synthesis; decreases hepatic VLDL synthesis	Cutaneous flushing, pruritus, gastrointestinal upset, liver function abnormalities, increased uric acid levels, increased glucose intolerance	Children: only short-term efficacy reported for homozygous FH; not recommended for routine use Adults: 1-3 g
Fibric Acid Derivatives: Gemfibrozil (Lopid), Clofibrate	Decreases hepatic VLDL synthesis; increases LPL activity	Increased incidence of gallstones and perhaps gastrointestinal cancer, myositis, diarrhea, nausea, rash, altered liver function, increased CPK levels, potentiation of warfarin	Children: not recommended Adults: gemfibrozil, 600-1200 mg; clofibrate, 1-2 g

CPK, creatine phosphokinase; FH, familial hypercholesterolemia; HDL, high-density lipoprotein; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A; LDL, low-density lipoprotein; LPL, lipoprotein lipase; VLDL, very-low-density lipoprotein

BOX 26-4

INDICATIONS FOR DRUG THERAPY FOR HYPERCHOLESTEROLEMIA IN CHILDREN AND ADOLESCENTS

1. Failure of diet therapy and lifestyle management for 6 to 12 months, *plus*
2. Age ≥ 10 years with one of the following lipid profiles and/or risk factors.
 - LDL cholesterol ≥ 190 mg/dL
 - LDL cholesterol 160-189 mg/dL with:
 - (1) a positive family history of premature CVD/events in first-degree relatives, or
 - (2) at least 1 high-level risk factor or risk condition, or
 - (3) at least 2 moderate-level risk factors or risk conditions.
 - LDL cholesterol 130-159 mg/dL with:
 - (1) at least 2 high-level risk factors or risk conditions, or
 - (2) at least 1 high-level risk factor or risk condition *plus* at least 2 moderate-level risk factors or risk conditions (Box 26-3).

OR

3. Children aged 8 or 9 years with LDL-C persistently ≥ 190 mg/dL together with *multiple* first-degree family members with premature CV disease/events, or the presence of at least 1 high-level risk factor or risk condition, or the presence of at least 2 moderate-level risk factors or risk conditions

From Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report, Pediatrics 128:S213-S256, 2011.

- c. Adverse effects of statins. Adverse effects of statins are infrequent but may include gastrointestinal upset, elevation of liver transaminases, and myopathy, ranging in severity from asymptomatic increases in creatine kinase (CK), to muscle aches or weakness, to fatal rhabdomyolysis. Myopathy and elevated liver enzymes are main concerns.
 - (1) More than a 10-time increase in CK levels and more than a 3-time increase in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels above the upper limits of normal are worrisome levels. Box 26-5 provides step-by-step instruction on initiation, titration, and monitoring of statin therapy (McGrindle et al, 2007).
 - (2) It is known that vigorous exercise, particularly contact sports or weightlifting, may result in an increase in CK level.
 - (3) Myopathy is defined as a serum CK level 10 times the upper limit of normal with or without muscle weakness or pain. Rhabdomyolysis is defined as unexplained muscle pain or weakness with a serum CK level of more than 40 times the upper limit of normal.
 - (4) Normal ranges of laboratory values are as follows (source: *Nelson's Textbook of Pediatrics*, 18th edition).
 - (a) CK: 5-130 U/L (adults)
 - (b) ALT: 5-45 U/L (1-19 yr)
 - (c) AST: 5-45 U/L (10-19 yr)
- d. Dosages of statins
 - (1) The starting dose of the statins is usually 10 mg (with the exception of Fluvastatin, 20 mg) given once daily at bedtime (see Table 26-5).

BOX 26-5**SUGGESTED INITIATION, TITRATION, AND MONITORING OF STATIN THERAPY IN CHILDREN AND ADOLESCENTS**

1. Measure baseline CK, ALT, and AST levels.
2. Start with lower dose given once orally at bedtime (see text for dosage).
3. Monitoring for potential adverse effects:
 - Instruct the patient to report *immediately* all potential adverse effects, especially myopathy (muscle cramps, weakness, asthenia, and more diffuse symptoms).
 - If myopathy is present, its relation to recent physical activities should be assessed, the medication stopped, and CK assessed.
 - The patient should be monitored for resolution of myopathy and any associated increases in CK.
 - Consideration can be given to restarting the medication once symptoms and laboratory abnormalities have resolved.
 - Advise female patients about concerns with regard to pregnancy and the need for appropriate contraception if warranted.
4. After 4 weeks, measure fasting lipoprotein profile, CK, ALT, and AST.
 - The threshold for worrisome level of CK is 10 times above the upper limit of reported normal; consider impact of physical activity.
 - The threshold for worrisome level of ALT or AST is 3 times above the upper limit of reported normal.
 - Target level for LDL: minimal, <130 mg/dL; ideal, 110 mg/dL.
5. At 4-week follow-up:
 - If target LDL levels achieved; no laboratory abnormalities:
 - Continue therapy and recheck in 8 wk and then 3 mo.
 - If laboratory abnormalities noted or symptoms reported:
 - Temporarily withhold the drug and repeat the blood work in ≈ 2 wk.
 - When anomalies return to normal, the drugs may be restarted with close monitoring.
 - If target LDL levels not achieved:
 - Increase the dose by 10 mg and repeat the blood work in 4 wk.
 - Continue stepped titration up to the maximum recommended dose until target LDL levels are achieved or there is evidence of toxicity.
6. Repeat laboratory tests every 3 to 6 months: fasting lipoprotein profile, CK, ALT, and AST.
7. Continue counseling on:
 - Compliance with medications and reduced fat diets.
 - Other risk factors, such as weight gain, smoking, and inactivity.
 - Counsel adolescent females about statin contraindication in pregnancy and the need for appropriate contraception. Seek referral to an adolescent medicine or gynecologic specialist as appropriate.

CK, creatine kinase; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Modified from McCrindle BW, et al: Drug therapy of high-risk lipid abnormalities in children and adolescents, *Circulation* 115:1948-1967, 2007.

- (2) The dose of statin is increased by 10 mg every 3 months to the $\frac{1}{2}$ or even the full adult dosage with periodic measurements of cholesterol. The maintenance dosage of the drug is decided by periodic determinations of cholesterol levels.
- (3) The minimal target level for LDL cholesterol is <130 mg/dL and the ideal target level is 110 mg/dL.

VII. HYPERTRIGLYCERIDEMIA

1. Significance of high triglyceride levels.
 - a. Hypertriglyceridemia is an independent risk factor for major coronary events after controlling for LDL-C and HDL-C.
 - b. Metabolic consequences of hypertriglyceridemia include (1) lowering of HDL-C, (2) production of smaller, denser LDL particles with more atherogenicity, and (3) a hypercoagulable state.
2. There are different cut-off points for treatment of hypertriglyceridemia in children and adults: 100 mg/dL for children <10 years; 130 mg/dL for ages 10 to 19 years; and 150 mg/dL for young adults (Tables 26-1 and 26-2).
3. Management of hypertriglyceridemia.
 - a. Diet therapy is the primary tool in treating high TG levels.
 - (1) Reduction of simple carbohydrate intake (and increased intake of complex carbohydrate), reduced saturated fat intake (such as CHILD-2-TG), and weight loss are associated with reduced levels of TG.
 - (2) It is important to know that both a high-fat diet and a high-carbohydrate diet raise TG levels. In fact, a diet high in carbohydrate, especially a high glycemic index diet, may be a more important source of hypertriglyceridemia than high fat intake. Therefore, all refined carbohydrate foods such as sugary drinks, cookies, ice cream, and after dinner deserts should be avoided and complex carbohydrates such as whole grain products should be consumed more.
 - b. Lifestyle changes with increased physical activity (at least 30 minutes of moderate-intensity exercise daily, 5 days a week) and weight control help reduce TG levels. Exercise will also help decrease LDL-C and increase HDL-C.
 - c. Dietary fish and fish oil. Omega-3 fatty acids in fish oils lower plasma TG levels by inhibiting the synthesis of VLDL cholesterol and TG in the liver. They also have antithrombotic properties.
 - (1) Children with increased TG levels (100 to 200 mg/dL) after a trial of lifestyle/diet management with CHILD-2-TG should increase dietary fish consumption.
 - (2) Children with fasting TG levels of ≥ 200 to 499 mg/dL, non-HDL levels of >145 mg/dL, after a trial of lifestyle/diet management with CHILD-2-TG and increased fish intake, may be considered for fish-oil supplementation. A prescription omega-3 fatty acid product (e.g., Omacor) 4 g/day and 8 g/day may be used. Most fish oil capsules contain only one third of the omega-3 fatty content contained in Omacor.

- d. Children with average fasting TG levels of ≥ 500 mg/dL or any single measurement of ≥ 1000 mg/dL should be treated in conjunction with a lipid specialist. For these patients, in addition to the dietary management with CHILD-2-TG and fish oil, use of fibrate or niacin should be considered to prevent pancreatitis.
 - (1) Fibrates have the effect of both lowering TG and raising HDL-C. Side effects seen in adults include myalgia, myositis, myopathy, rhabdomyolysis, liver toxicity, gallstones, and glucose intolerance. Safety and efficacy data in children are limited. CK level and liver enzymes should be monitored every 3 months.
 - (2) Niacin is the best known drug that raises HDL-C but it also reduces triglyceride levels. Adverse effects of niacin include liver toxicity, GI tract upset, and facial flushing. Less commonly seen side effects are hyperuricemia and glucose intolerance. Extended-release preparations produce less flushing but are more likely to produce liver toxicity. Niacin is rarely used to treat the pediatric population because of reported poor tolerance and the potential for very serious adverse effects. Liver transaminases should be checked every 3 months.

VIII. LOW HDL LEVEL

1. Significance of low HDL-C level.
 - a. Low levels of HDL-C represent a major CV risk factor. Despite the presence of desirable total cholesterol (TC) levels, patients with low HDL-C may be at high risk of developing CV events.
 - b. HDL-C has a number of antiatherogenic effects. The best known of these relates to the ability of HDL-C to promote the efflux of cholesterol from macrophages in the arterial wall, through reverse cholesterol transport.
 - c. Low HDL-C level is defined as <40 mg/dL in adolescent boys and girls. In adults, low HDL level is defined as <40 mg/dL in men and <50 mg/dL in women.
2. Management of low levels of HDL cholesterol.
 - a. Primary approach in managing low levels of HDL cholesterol is lifestyle change and diet therapy. The following has been suggested for adult patients with low levels of HDL-C.
 - (1) Lifestyle change with regular exercise (30 minutes of brisk aerobic exercise every day or every other day) is recommended. Weight control (and quitting smoking) is equally important.
 - (2) Dietary intervention.
 - (a) Diets low in saturated fat and rich in the polyunsaturated fatty acids are recommended. This is because the most effective way to reduce CV risk in patients with low HDL levels is to maintain low LDL-C levels, not because it raises HDL levels.
 - (b) Consumption of high glycemic index foods should be restricted.
 - (c) Omega-3 fatty acids may help raise HDL levels.

- b. Current pharmacologic options for adults include nicotinic acid (niacin), fibrates, and statins but none of them are without major adverse effects. The use of drugs should be considered only when all nonpharmacologic measures do not achieve the goal of raising HDL-C level in pediatric patients.
- (1) Niacin (nicotinic acid or vitamin B₃) is the most effective medication for raising HDL-C (raising HDL level by 20% to 35%). However, niacin is rarely used in the pediatric population because of the potential for serious adverse effects. One of the major adverse effects of niacin is severe flushing. A newer extended release formulation of niacin (Niaspan) may reduce flushing substantially but it is more likely to increase liver toxicity. Flushing (which may involve prostaglandin D₂) can be blocked by taking aspirin 300 mg half an hour before taking niacin.
 - (2) Fibrate therapy is also effective, producing an average increase of HDL by 10% to 25%. Statins are the least effective of the three drug classes in raising HDL levels.

Chapter 27

Preventive Cardiology

27

Atherosclerotic cardiovascular disease is a major cause of morbidity and mortality and is responsible for more than 50% of all the deaths in the United States. Among established cardiovascular (CV) risk factors are dyslipidemia, which includes high concentrations of LDL-C and triglycerides (TG), and a low concentration of HDL-C. These lipid disorders are presented in Chapter 26. Obesity has been shown to be a CV risk factor. To reduce CV death, it is logical to start efforts to prevent and correct known risk factors during childhood.

There is now clear evidence that atherosclerotic lesions start to develop in early childhood and progress to irreversible lesions in adolescence and adulthood. The strongest evidence of childhood onset of coronary artery disease (CAD) comes from the Bogalusa Heart Study and the Pathological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Autopsy studies found that atherosclerosis originates in childhood, with a rapid increase in the prevalence of coronary pathology during adolescence and young adulthood. Fatty streak, the earliest lesion of the atherosclerosis, occurred by 5 to 8 years of age, and fibrous plaque, the advanced lesion, appeared in the coronary arteries in subjects in their late teens. Fibrous plaque was found in over 30% of 16- to 20-year-olds and the prevalence of the lesion reached nearly 70% by age 26 to 39. These studies also confirmed that the extent of pathologic changes in the aorta and coronary arteries increased with age and so did the number of known CV risk factors that the individual had at the time of death.

The traditional risk factors for CAD include positive family history of coronary heart disease, smoking, high levels of cholesterol, low levels of HDL cholesterol, hypertension, and diabetic or prediabetic states (**Box 27-1**). A family history of CAD in the first-degree relatives (parents and siblings) has been found to be the single best predictor of CV risk for adults. Unlike in adults, family history for children includes the first- and second-degree relatives (including parents, grandparents, and blood-related aunts and uncles) who have or had CAD before age 55 for males and before age 60 for females. The reason for this is because some children's parents are too young to have developed clinical CAD when their children are examined. Obtaining history of these cardiovascular risk factors should be a routine process in the practice of medicine.

A. Obesity and Its Comorbidities as CV Risk Factors

Recent studies have shown that obesity is a risk factor for CAD independently of the standard risk factors, probably through the emerging risk factors. The

BOX 27-1**MAJOR RISK FACTORS FOR CORONARY HEART DISEASE**

- Family history of premature coronary heart disease, cerebrovascular or occlusive peripheral vascular disease (with onset before age 55 years for men and 65 years for women in parents or grandparents)
- Cigarette smoking
- Hypercholesterolemia
- Hypertension (BP >140/90 or on antihypertensive medication)
- Low levels of high-density lipoprotein (<40 mg/100 mL)
- Diabetes mellitus (as a coronary heart disease risk equivalent)

Adapted from Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Education, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report, *Circulation* 106:3143-3421, 2002.

emerging risk factors, which are commonly found in obese persons, include (1) atherogenic dyslipidemia (also known as “lipid triad”), which consists of raised levels of TG and small LDL particles and low levels of HDL-C; (2) insulin resistance (hyperinsulinemia), (3) a proinflammatory state (elevation of serum high-sensitivity C-reactive protein), and (4) a prothrombotic state (increased amount of plasminogen activator inhibitor-1 [PAI-1]). The cluster of these risk factors occurring in one person is known as the “metabolic syndrome.” In metabolic syndrome, LDL-C levels may not be elevated but apolipoprotein B (apoB) and small LDL particles are elevated; the smallest particles in the LDL fraction are known to have the greatest atherogenicity. This syndrome occurs more commonly in individuals with abdominal (visceral) obesity. With increasing adiposity, the lipid triad becomes more pronounced. Hispanics and South Asians seem to be particularly susceptible to the syndrome.

Clinically identifiable components of metabolic syndrome for adults and children are listed in [Box 27-2](#). Several definitions for diagnosis of metabolic syndrome in children were proposed in the past with different cut-off points for fasting glucose and triglycerides (TG). However, one proposed by the International Diabetes Federation (2007) appears to be the best because it is based on more recent NHANES data (collected between 1988 and 2002) and shows the same cut-off points of glucose and TG for adults and children. The presence of at least three of the risk factors is required to make the diagnosis of metabolic syndrome in adults and children. Other components of metabolic syndrome, such as proinflammatory and prothrombotic states, are not routinely measured in clinical practice. C-reactive protein ≥ 3 mg/L may be significant in adults. The prevalence of metabolic syndrome in overweight adolescents is about 30% to 50%.

Waist circumference (reflecting visceral adiposity) is a better predictor of CV disease than body mass index (BMI). There is a significant difference in waist circumference according to ethnicity and gender. Ethnicity- and gender-specific waist circumference percentiles are now available for children (see Tables C-1 through C-3, Appendix C). In general, Mexican American boys and girls have higher waist circumference than other ethnic groups.

BOX 27-2

DEFINITIONS OF METABOLIC SYNDROME IN ADULTS AND IN CHILDREN AND ADOLESCENTS

	ADULTS^a	CHILDREN AND ADOLESCENTS^b
Obesity (waist circumference)	Men: WC ≥40 inches (102 cm) Women: WC ≥35 inches (88 cm)	WC ≥90th percentile or adult cut-off point
Triglycerides	≥150 mg/dL	≥150 mg/dL
HDL cholesterol	Men <40 mg/dL Women <50 mg/dL	≤40 mg/dL
Hypertension	130/85 mm Hg or greater	Systolic ≥130; diastolic ≥85 mm Hg
Elevated fasting glucose	≥100 mg/dL	≥100 mg/dL
The presence of at least three of the above abnormalities constitutes metabolic syndrome.		

BMI, body mass index; BP, blood pressure; WC, waist circumference.

^aThe Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Education, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report, *Circulation* 106:3143-3421, 2002.

^bZimmet P, Alberti G, Kaufman F, et al: International Diabetes Federation Task Force on Epidemiology and Prevention of Diabetes. The metabolic syndrome in children and adolescents, *Lancet* 369(9579):2059-2061, 2007.

Prevention of metabolic syndrome may prevent CAD. The mainstay of prevention is achieving optimum weight, normal BP, and normal lipid profile by dietary intervention and promotion of an active lifestyle. Each component of metabolic syndrome present should be treated aggressively to reduce CV risk factors and to prevent diabetes. Pharmacologic intervention is usually not required in children, but drugs may be used on selected high-risk patients.

Weight reduction is of prime importance in managing metabolic syndrome. All successful pediatric weight management programs include four components: (1) dietary, (2) exercise, (3) behavior modification, and (4) family components. Among these, dietary intervention and regular exercise combined are the cornerstones of weight management. Only through behavior modification can long-term healthy eating and activity patterns be established; attempts at employing diet and exercise for quick weight loss usually fail. Without involvement of the parents and family, behavior modification of children and adolescents is difficult to achieve. Consultations with registered dietitians, psychologists, and/or exercise specialists may be sought or a referral to a multidisciplinary weight management program may become necessary.

B. Cigarette Smoking as a Cardiovascular Risk Factor

Cigarette smoking is a powerful independent risk factor for myocardial infarction, sudden death, and peripheral vascular disease. Even passive exposure to smoke causes alterations in the risk factors in children.

The prevalence of cigarette smoking nationwide among high school students remains high. Current use of any tobacco product ranges from 13% among middle school students to 28% among high school students. Among college students, 33% are current users of tobacco products and nearly 50% used a tobacco product in the past year. More recent national data show that about 20% of high school students and 12% of middle school students are tobacco users. There are usually smokers in the household of middle school and high school student smokers.

Physicians should assess the status of smoking, provide smoking prevention messages, and help counsel parents and children about smoking cessation. The following are some pathophysiologic effects of smoking on the CV system, which physicians can use in counseling their patients to stop smoking. All of the pathophysiologic effects are involved in accelerating atherosclerosis in the coronary and peripheral arteries or increasing the probability of thrombosis (with potential for stroke).

1. Atherogenic dyslipidemia, with increasing LDL-C, VLDL-C, and TG levels and lowering HDL-C levels.
2. Prothrombotic predisposition, increasing levels of fibrinogen, factor VII, and other factors involved in the fibrin clotting cascade and decreasing the concentration of plasminogen. It also activates platelets, increasing their ability to adhere to the vessel wall.
3. Increase in blood viscosity by increasing hemoglobin levels (through carbon monoxide–induced increase in carboxyhemoglobin) and by an elevation of plasma fibrinogen levels.
4. Acceleration of atherosclerotic process by increasing monocyte adhesion to endothelial cells (the initial step in atherogenesis), by decreasing nitric oxide synthesis (with resulting endothelial dysfunction), and by decreasing synthesis of prostacycline.
5. Peripheral arterial disease through endothelial dysfunction.
6. Increase in BP, heart rate, and myocardial oxygen consumption (by stimulation of sympathetic nervous system).

C. Practice of Preventive Cardiology

Atherosclerotic cardiovascular disease has its onset during childhood. The prevalence of obesity is increasing during childhood along with its comorbidities, including metabolic syndrome (see [Box 27-2](#)). Intervention to reduce the CV risk factors in childhood has been successful with low-calorie diets, smoking prevention, increasing physical activities, and family-based weight control programs. This is due to the fact that some of the risk factors are detectable, modifiable, or treatable.

1. Although positive family history of CV disease is not modifiable, its presence is a marker for a high risk of heart disease. A history of premature CAD in the first- or second-degree relatives (parents, siblings, grandparents, or blood-related aunts and uncles) before age 55 for males and before age 60 for females should prompt physicians to check on other risk factors.

2. Hypercholesterolemia is one of the major identifiable and treatable risk factors.
3. Hypertension is also an identifiable and treatable risk factor.
4. Other risk factors, such as smoking, consumption of atherogenic diets, and physical inactivity, are all modifiable by behavior changes.
5. Obesity is easily detectable. Although treatment of obesity can be frustrating to both patient and physician, patient education and behavior modification can be productive.
6. Inclusion of HbA_{1c} should be considered in the screening protocol to detect diabetic or prediabetic state.

The American Heart Association has published a guideline for the prevention of CV disease. [Table 27-1](#) is a summary of the recommendations which provides treatment goals and recommendations to achieve the goals of reducing CV risks in children and adolescents identified as high risks for future CV disease.

TABLE 27-1

SUMMARY GUIDELINES FOR PREVENTIVE PEDIATRIC CARDIOLOGY

RISK IDENTIFICATION	TREATMENT GOALS	RECOMMENDATIONS
Blood Cholesterol Total cholesterol: >170 mg/dL is borderline >200 mg/dL is elevated LDL-C: >110 mg/dL is borderline >130 mg/dL is elevated	LDL-C: <130 mg/dL (<110 mg/dL is even better) For patients with diabetes, LDL-C <100 mg/dL	If LDL-C is above goals, initiate additional therapeutic lifestyle changes, including diet (<7% of calories from saturated fat; <200 mg cholesterol per day), in conjunction with a trained dietitian. Consider LDL-lowering dietary options (increase soluble fiber by using age [in years] plus 5 to 10 g up to age 15, when the total remains at 25 g per day) in conjunction with a trained dietitian. Emphasize weight management and increased physical activity. If LDL-C is persistently above goals, evaluate for secondary causes (thyroid-stimulating hormone, liver function tests, renal function tests, urinalysis). Consider pharmacologic therapy for individuals with LDL >190 mg/dL with no other risk factors for CVD or >160 mg/dL with other risk factors present (blood pressure elevation, diabetes, obesity, strong family history of premature CVD). Pharmacologic intervention for dyslipidemia should be accomplished in collaboration with a physician experienced in treatment of disorders of cholesterol in pediatric patients.
Other Lipids and Lipoprotein Triglycerides: >100 mg/dL is elevated for <10 yr >130 mg/dL is elevated for >10 yr HDL-C: <40 mg/dL is reduced	Fasting triglycerides: <75 mg/dL for <10 yr <90 mg/dL for >10 yr HDL-C >40 mg/dL	Elevated fasting TG and reduced HDL-C are often seen in the context of overweight with insulin resistance. Therapeutic lifestyle change should include weight management with appropriate energy intake and expenditure. Decrease intake of simple sugars. If fasting TG is persistently elevated, evaluate for secondary causes such as diabetes, thyroid disease, renal disease, and alcohol abuse. No pharmacological interventions are recommended in children for isolated elevation of fasting TG unless this is very marked. Treatment may be initiated at TG >400 mg/dL to protect against postprandial TG of 1000 mg/dL or greater, which may be associated with an increased risk of pancreatitis.

TABLE 27-1

SUMMARY GUIDELINES FOR PREVENTIVE PEDIATRIC CARDIOLOGY (Continued)

RISK IDENTIFICATION	TREATMENT GOALS	RECOMMENDATIONS
Blood Pressure Systolic and diastolic pressure: >95th percentile for age, sex, and height	Systolic and diastolic blood pressure <95th percentile for age, sex, and height	Promote achievement of appropriate weight. Reduce sodium in the diet. Emphasize increased consumption of fruits and vegetables. If BP is persistently above the 95th percentile, consider possible secondary causes (e.g., renal disease, coarctation of the aorta). Consider pharmacologic therapy for individuals above the 95th percentile if lifestyle modification brings no improvement and there is evidence of target-organ changes (left ventricular hypertrophy, microalbuminuria, retinal vascular abnormalities). Start blood pressure medication individualized to other patient requirements and characteristics (i.e., age, race, need for drugs with specific benefits). Pharmacologic management of hypertension should be accomplished in collaboration with a physician experienced in pediatric hypertension.
Weight BMI: >85th percentile is overweight >95th percentile is obese	Achieve and maintain BMI <95th percentile for age and sex	For children who are overweight (>85th percentile) or obese (>95th percentile), a weight management program should be initiated with appropriate energy balance achieved through changes in diet and physical activity. Use the “5-2-1-0” message and “MyPlate” for education and counseling. For children of normal height, a secondary cause of obesity is unlikely. Weight management should be directed at all family members who are overweight, using a family-centered, behavioral management approach. Weight management should be done in collaboration with a trained dietitian.

Diabetes

Fasting plasma glucose:
 ≥ 126 mg/dL

Near normal fasting plasma glucose
 (< 120 mg/dL)
 Near normal HgA_{1c} ($< 7\%$)

Management of type 1 and type 2 diabetes in children and adolescents should be accomplished in collaboration with a pediatric endocrinologist.

For type 2 diabetes, the first step is weight management with improved diet and exercise.

Because of risk for accelerated vascular disease, other risk factors (e.g., blood pressure, lipid abnormalities) should be treated more aggressively in patients with diabetes.

Cigarette Smoking

Complete cessation of smoking for children and parents who smoke

Advise every tobacco user (parents and children) to quit, and be prepared to provide assistance with this (counseling/referral to develop a plan for quitting using available community resources to help with smoking cessation).

Modified from Kavey RW, Daniels SR, Lauer RM, et al: American Heart Association Guidelines for Primary Prevention of Atherosclerotic Cardiovascular Disease Beginning in Childhood, *Circulation* 107:1562-1566, 2003.

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PART VII

CARDIAC SURGICAL PATIENTS

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Pre- and Postoperative Management

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The current trend is to carry out total repair of CHDs at an early age whenever such repair is technically possible. Early total repair may obviate the need for palliative procedures. This may also prevent pulmonary vascular disease or permanent damages to the cardiovascular system, which is known to develop in certain CHDs. However, recommendations for the timing and type of operation vary from institution to institution. The improved results currently seen with pediatric cardiac surgery are in part attributed to improved operative techniques and cardiopulmonary bypass (CPB) methods. In addition, the coordinated multidisciplinary approach has contributed to significant decrease in perioperative morbidity and mortality.

Open heart procedures use CPB with some degree of hypothermia and a varying duration of low flow or circulatory arrest. Open procedures are required for repair of intracardiac anomalies (e.g., VSD, TOF, TGA). Closed procedures do not require CPB; they are performed for repair of extracardiac anomalies (e.g., COA, PDA) or palliative procedures (e.g., B-T shunt procedures or PA banding). The following sections outline some basic aspects of pre- and postoperative management of cardiac patients for pediatricians.

I. PREOPERATIVE MANAGEMENT

Good preoperative preparation including complete delineation of cardiac anatomy and assessment of hemodynamics is mandatory for a smooth operative and postoperative course. Some infants require preoperative stabilization with prostaglandin E₁ (continuous IV drip at 0.01-0.1 mcg/kg/min) to maintain ductus arteriosus patency while others may need inotropic and lusitropic support. Patients with TGA and restrictive PFO may require balloon atrial septostomy.

1. All children should have a careful history and physical examination within a few days before the procedure. This is to gain full understanding of chronic medical problems (e.g., renal dysfunction, asthma) and to uncover acute medical problems (e.g., upper and lower respiratory, and urinary tract infections) that would mandate rescheduling of elective surgeries.
2. Laboratory evaluation
 - a. Complete blood count, urinalysis, serum electrolytes and glucose, blood urea nitrogen (BUN), and serum creatinine of all cardiac patients are routinely obtained.
 - b. Chest radiography and ECG of all patients are obtained.

- c. Head and renal ultrasound is performed in all neonates with significant congenital heart defects.
 - d. For open heart procedures, blood coagulation studies—prothrombin time (PT), activated partial thromboplastin time (aPTT), and platelet count—are obtained.
 - e. If necessary, blood should be collected for chromosome studies (karyotyping, fluorescence in situ hybridization, and DNA microarray) preoperatively.
3. Patients undergoing CPB whose weight is more than 3.5 kg are cross-matched for 4 units of packed red blood cells (PRBCs) and those weighing less than 3.5 kg are cross-matched for 2 units of whole blood. One to two units of PRBCs are cross-matched for those undergoing closed procedures. One to four units of platelets are needed for the procedure additionally. Irradiated blood products will be required for immunocompromised patients (e.g., patients with suspected or confirmed chromosome 22 microdeletion).
4. Medications
- a. At some institutions, angiotensin-converting enzyme (ACE) inhibitors are withheld 12 hours prior to the planned surgery in an effort to minimize anesthesia-induced refractory hypotension during anesthesia induction.
 - b. Diuretics are discontinued 8 to 12 hours preoperatively (or this may be individualized).
 - c. Digoxin is discontinued after the evening dose.
 - d. Antiarrhythmics are continued at the same dosage until immediately before the surgery.
 - e. Nonsteroidal antiinflammatory drugs (e.g., aspirin, ibuprofen) and antiplatelet drugs (e.g., dipyridamole) are discontinued 7 to 10 days prior to surgery.
 - f. Warfarin is discontinued 4 days prior to the planned operation. If the patient is at high risk for thromboembolism, continuous heparin drip is started 2 days prior to the operation and the infusion rate is adjusted to maintain an aPTT of 60 to 85 sec.
5. Prevention of infection: Broad-spectrum antibiotics are used to decrease the risk of perioperative infection. Duration of antibiotic regimen is institution dependent but can be individualized based on the patient's age, condition, and comorbidities.
- a. Vancomycin, 10-15 mg/kg/dose IV every 6 to 8 hours (maximum dose 4 g/day).
 - b. Clindamycin, 10 mg/kg/dose (adolescents/adults: 600 mg/dose) IV every 6 to 8 hours, starting immediately prior to surgery, is the recommended regimen at some institutions.
 - c. Neonates who already are on ampicillin and gentamicin are continued on these drugs.
 - d. Thin layer of mupirocin 2% ointment is applied to both nostrils to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) colonization.
6. For older children, the emotional preparation for surgery is as important as the physical preparation.

II. POSTOPERATIVE CARE OF CARDIAC PATIENTS

A high level of vigilance for signs of complications should be maintained during the postoperative period so that appropriate therapy can be initiated early.

A. Normal Convalescence

Physicians should be familiar with the postoperative course of normally recovering patients in order to recognize abnormal convalescence.

1. General care: Successful postoperative management requires accurate monitoring and documentation of the patient's vital signs, medication administration, and laboratory results. Vital signs including heart rate, arterial or noninvasive blood pressure, oxygen saturation, and respiratory rate are monitored closely (e.g., every 15 to 60 min). Urine and chest tube outputs, end-tidal or transcutaneous CO₂, central venous pressure, and, at times, right and left atrial and pulmonary arterial pressures are recorded meticulously. All administered medications, enteral or parenteral fluids, and blood products are documented. Fluid balance is monitored continuously. Laboratory results and their trends are charted for review electronically.
2. Pulmonary system
 - a. Arterial blood gases are in the acceptable normal range.
 - b. Chest radiography shows no evidence of pneumothorax, atelectasis, pleural effusion, or elevation of hemidiaphragm.
3. Cardiovascular system
 - a. Warm skin, full peripheral pulses with brisk capillary refill, normal blood pressure (BP), and an adequate urine output (at least 1 ml/kg/hr) are clinical evidence of good cardiac output. Decrease in expected systemic venous saturation is a sensitive predictor of low cardiac output. A normal systemic arterial-to-venous oxygen saturation difference of less than 30% is indicative of good cardiac output.
 - b. Mild arterial hypertension is present in the early postoperative period following CPB (due to increased levels of catecholamines, plasma renin, or angiotensin II).
 - c. Cardiac rhythm should be sinus and the heart rate relatively high. Ranges of heart rate (beats/min) in normally convalescing postoperative patients are as follows:

Less than 6 months	110 to 190
6 to 12 months	100 to 170
1 to 3 years	90 to 160
Over 3 years	80 to 150
4. Renal system: Adequate urine output (i.e., above 1 mL/kg/hr) and evidence of adequate solute excretion (e.g., serum K⁺ below 5 mEq/L; BUN below 40 mg/dL; creatinine below 1 mg/dL) are signs of normal renal function.
5. Metabolic system
 - a. Retention of water and sodium and depletion of whole-body potassium are commonly seen following open heart surgeries. They result

in mild hyponatremia and hypokalemia, and a 5% weight gain. In anticipation of fluid overload, mechanical ultrafiltration is performed in selected cases intraoperatively.

- b. Mild metabolic acidosis (with a base deficit of -4 mEq/L) associated with mild lactic acidemia is common in the first few hours after CPB and does not usually require treatment.
- c. Varying degrees of fever are nearly always present during the first few days, and extensive workup for infection is not indicated. Causes of fever include reaction to CPB, reaction to homologous blood, atelectasis, pleural effusion, low cardiac output, infection, and brain stem damage.
6. Gastrointestinal system: As the splanchnic circulation receives over 25% of total cardiac output avoidance of low cardiac output syndrome is the principal strategy to avoid gastrointestinal (GI) dysfunction. Feedings are started after the patient becomes hemodynamically stable and are advanced as tolerated. Daily caloric count and its adjustment are crucial. H_2 -receptor antagonists (ranitidine, 1 mg/kg/dose IV every 6 to 8 hours) or proton pump inhibitors (e.g., esomeprazole 0.5-1 mg/kg/dose IV every 24 hours, maximum pediatric dose 20 mg/day) are initiated for gastric protection.
7. Hematologic system: Clotting studies should be normal, and hemoglobin should be at least 9.5 g/dL or higher depending on the patient's age, cardiac anatomy, and surgical procedure.
8. Neurologic system: The patient should respond appropriately for the level of sedation without evidence of neurologic defects (e.g., hemiplegia, visual field defects) or seizures. Near infrared spectroscopy (NIRS) for transcranial cerebral oximetry is a noninvasive method to monitor frontal lobe oxygen metabolism. Cerebral oxygen saturation, measured by NIRS, is a composite of the oxygen saturation in combined cerebral arterial and venous vascular bed (arterial and venous blood flow ratio of $\approx 25:75$, with negligible capillary blood). It is a helpful method to detect cerebral hypoxia during low cardiac output states.

B. Care Following Uncomplicated Operation

Postoperative care in congenital cardiac surgery is unique due to the complexity and heterogeneity of cardiac defects and the wide age range of patients. Furthermore, the guidelines for postoperative management differ from institution to institution, making this task even more complicated. Although the following recommendations are only one set of these guidelines, one aspect of successful management remains the same: anticipation of possible complications (e.g., decrease of cardiac index 6 to 12 hours postoperatively; pulmonary hypertension in association with particular defects; arrhythmias after specific surgeries, etc.).

1. General care

- a. Fluid replacement: Because of the tendency to retain sodium and water, a minimal amount of dextrose in water without ($D_{10}W$ in infants, D_5W in children) or with only a small amount of sodium ($D_{10} \frac{1}{4}NS$, $D_5 \frac{1}{4}NS$) is administered for approximately 48 hours after

surgery. A modest amount of potassium (e.g., KCL, 4 mEq/100 mL IV fluids) is given on the first day of surgery. Recommended fluid volume in the first 24 hours after open procedures is 50% of maintenance volume with gradual increase over the following postoperative days to 60% and then to 75%.

- b. The patient should receive medications for adequate analgesia and sedation. For pain relief fentanyl (IV drip at 1-3 mcg/kg/hr or 1-2 mcg/kg/dose IV every 30 to 60 min) or morphine sulfate (IV drip at 0.01-0.05 mg/kg/hr or 0.1-0.2 mg/kg/dose IV every 2 to 4 hours, maximum dose 15 mg/dose) are commonly used. Sedation is achieved by administration of midazolam (0.05-0.15 mg/kg/dose IV every 1 to 2 hours or IV drip at 1-2 mcg/kg/min) or other benzodiazepams.

2. Pulmonary system

- a. Extubated patients should show no signs of respiratory distress (grunting, nasal flaring, and retraction). Good chest expansion and evidence of good air exchange to both lungs should be present. Depending on the hemodynamics or cardiopulmonary pathophysiology, patients may be administered supplemental oxygen via nasal cannula or face mask. Pulmonary physiotherapy (consisting of incentive spirometry, coughing and deep breathing exercise, and chest percussion with postural drainage) is administered as necessary.
- b. In intubated patients, chest radiographs are obtained to check the position of chest tubes and central and arterial lines and to check for evidence of pneumothorax, atelectasis, pleural effusion, or mainstem bronchus intubation. Significant degrees of pneumothorax or pleural effusion may require treatment. Widening of the mediastinal shadow suggests accumulation of blood and requires investigation of the function of the mediastinal chest tube.

In the first postoperative days, the goal of ventilation is to maintain adequate arterial partial pressure of oxygen (P_{aO_2}) and mild respiratory alkalosis along with an arterial partial pressure of carbon dioxide (P_{aCO_2}) between 28 and 35 mm Hg (all to decrease PVR). Hyperventilation (P_{aCO_2} below 28 mm Hg) is corrected by decreasing the ventilator rate, decreasing the tidal volume, and adding dead space (5-10 mL at a time) to the airway. Hypoventilation is corrected by the opposite maneuvers. Low P_{aO_2} is corrected by raising the F_{iO_2} , adding positive-end expiratory pressure (PEEP), or increasing tidal volume. Physiologic PEEP of 3-5 cm H_2O is used in children. The use of high mean airway pressure or high levels of PEEP may increase PVR and decrease cardiac output; both should be avoided in a patient who has had Senning procedure or cavopulmonary anastomosis (e.g., Glenn or Fontan operation).

Tracheal toilet is carried out through the endotracheal tube every 2 hours, or more often if necessary. It consists of instillation of 0.5-5 mL of saline and suctioning of both mainstem bronchi and bag ventilation for 1 to 2 min with oxygen (F_{iO_2} 1) immediately before and after suctioning.

- c. Extubation is performed as soon as possible, usually in the operating room in children undergoing closed procedures, within 4 to 8 hours after uncomplicated open heart procedures, and the day after complex open procedures. Criteria for extubation include the following:
 - (1) The patient should be awake and alert, and should have a favorable nutritional status.
 - (2) The patient should be breathing well, with a satisfactory spontaneous respiratory rate for age and no use of accessory respiratory muscles. Ideally, vital capacity should be more than 15 mL/kg. On minimal ventilatory support (FiO_2 no more than 0.4, tidal volume at 8-10 mL/kg, and PEEP no more than 5 cm H_2O), there should be adequate PaO_2 and no evidence of acidosis or hypercapnia.
 - (3) The patient should be in a reasonable and stable hemodynamic state (normal BP, adequate cardiac output, no significant arrhythmias). There should be no significant pneumothoraces or pleural effusions. The patient should not have important bleeding and should have minimal chest tube drainage.
 - (4) Postextubation laryngeal edema is treated with racemic epinephrine (2.25% solution; 0.125-0.5 mL diluted with 3 mL of water or normal saline given via nebulizer).
- d. Postoperative *pulmonary hypertensive crisis* leads to decreased cardiac output and, if untreated, may be fatal. The best strategy is prevention. Measures to prevent pulmonary hypertensive crisis are important for patients who had severe pulmonary arterial hypertension preoperatively. The following are recommended:
 - (1) Adequate analgesia and sedation.
 - (2) Paralysis by vecuronium bromide (continuous IV drip at 0.05-0.15 mg/kg/hr or intermittent IV infusion of 0.05-0.1 mg/kg/dose every 60 min) or pancuronium bromide (continuous IV drip at 0.02-0.1 mg/kg/hr or intermittent IV infusion of 0.05-0.1 mg/kg/dose every 30 to 60 min).
 - (3) Supplemental oxygen.
 - (4) Avoidance of hypercapnia.
 - (5) Low PEEP.
 - (6) Maintaining alkalotic pH.
 - (7) Avoidance of deep and vigorous tracheal aspiration.
 - (8) Administration of inhaled nitric oxide (selective pulmonary vasodilator) at 5-40 parts per million (usual range 5-20 parts per million).
 - (9) Intravenous vasodilators (α -adrenergic antagonists, phosphodiesterase inhibitors, nitrovasodilators, and prostaglandins) may be considered. However, it should be noted that essentially all these agents dilate the systemic vasculature as well, leading to systemic hypotension.
- 3. Cardiovascular system: Complete correction of the intracardiac defect and adequate intraoperative myocardial protection generally will result

in good cardiac function. Signs of reduced cardiac output, abnormal blood pressures, abnormal heart rate, and abnormal rhythm should be monitored continually.

- a. *Low cardiac output syndrome* (LCOS) is the most serious condition of abnormal convalescence. Signs of LCOS include systemic vasoconstriction (poor perfusion, cold extremities, weak pulses), resting tachycardia, oliguria, pulmonary venous congestion (rales, rhonchi), and systemic venous congestion (hepatomegaly, anasarca, ascites). Systemic hypotension may be a late result of LCOS and is an ominous sign. Laboratory findings include metabolic acidosis, lactic acidemia, azotemia, reduced creatinine clearance, rising serum K⁺, decreased partial central venous pressure of oxygen (PvO₂) below 30 mm Hg from RA or central venous line, and increased arterial-to-venous oxygen saturation difference of more than 40%.

Inadequate cardiac output may be caused by (1) low preload, (2) high afterload, (3) depressed myocardial contractility, (4) cardiac tamponade, (5) arrhythmias including sinus bradycardia or sinus tachycardia, (6) inadequate surgical repair, (7) pulmonary hypertension, and (8) insufficient ventilation. Treatment is directed at the cause.

- (1) Low preload may be due to intravascular volume depletion (manifested by decreased RA and LA pressures) or due to diminished blood flow to LV (e.g., pulmonary venous obstruction, PA hypertension, PS, or RV failure in the absence of adequate intraarterial shunting; evident by elevated RA and decreased LA pressure). In the case of MS which also decreases LV preload, RA and LA pressures are both elevated. Though all these conditions ultimately reduce the LV preload and subsequently the cardiac output, treatment is specific to each condition. Low intravascular volume is treated with IV crystalloid or colloid to increase the intravascular volume to raise central venous pressure to 10-15 mm Hg. Other conditions are treated by eliminating the cause.

- (2) High afterload (with increased SVR) may be caused by hypoxia, acidosis, hypothermia, or pain. In addition to the correction of the cause, the elevated SVR is treated with afterload reduction.

- (a) Phosphodiesterase inhibitors (e.g., milrinone) play a crucial role in treatment of LCOS. They not only have a vasodilatory effect, but also lusitropic and inotropic effects without being arrhythmogenic. These effects occur without an increase in myocardial oxygen consumption. Milrinone is usually initiated in the operating room and is continued as an IV drip at a rate of 0.1-1 mcg/kg/min (usual range 0.25-0.75 mcg/kg/min) postoperatively.

- (b) Nitroprusside (IV drip at 0.3-10 mcg/kg/min) or nitroglycerin (IV drip at 0.5-6 mcg/kg/min) can be used to further reduce elevated SVR. Both agents have a favorable effect on PVR.

In addition, nitroglycerin is a potent coronary vasodilator, which may be beneficial after arterial switch operation.

- (c) Phenoxybenzamine, a long-acting α -adrenergic blocking agent, is used in selected postoperative patients at some centers.
- (3) Depressed myocardial contractility (demonstrated by echo) may be treated by optimizing arterial oxygen saturation; by addressing anemia, hypocalcemia, and/or acidemia; and by administration of inotropic agents. The optimal oxygenation is achieved by maintaining a patent airway with good respiratory care, adjusting FiO_2 if necessary, reducing pulmonary shunting by the use of PEEP, and reducing pulmonary edema by the use of diuretics. The following inotropic agents may be used:
 - (a) Epinephrine (continuous IV drip at a rate of 0.01-0.05 mcg/kg/min; low dose to minimize undesirable α -agonist effects).
 - (b) Dopamine (continuous IV drip, starting at 2.5 mcg/kg/min and increasing up to 10 mcg/kg/min if necessary).
 - (c) Milrinone (by inhibition of type-III phosphodiesterase increases intracellular cAMP which ultimately augments myocardial contractility) is started with or without a loading dose of 50 mcg/kg and is maintained at an infusion rate of 0.1-1 mcg/kg/min.
- (4) Cardiac tamponade is treated with urgent decompression of the pericardial space. Early cardiac tamponade results from persistent surgical bleeding not properly drained by the chest tubes; it may even occur when the pericardium is removed or left widely open. It must be suspected when the chest tube drainage abruptly decreases or stops in a patient with previously significant bleeding. Characteristically, the patient is tachycardic and hypotensive with narrowed pulse pressure. Atrial pressures are elevated. Response to volume administration and inotropic agents is minimal. Chest radiographs show widening of the cardiac silhouette. Echo demonstrates pericardial effusion and diastolic collapse of the RA and RV, sensitive indicator of tamponade. Cardiac tamponade requires prompt pericardiocentesis or surgical exploration for evacuation of the pericardial hematoma or control of bleeding by urgent opening of the sternotomy, often in the intensive care unit.
- (5) Sinus bradycardia or tachycardia may be detrimental in a postoperative patient with limited cardiac reserve.
 - (a) Attention to detail is necessary to unmask secondary causes of sinus bradycardia such as medication interaction, hypoxia, hypoglycemia, electrolyte imbalance, increased intracranial pressure, and hypothyroidism. Injury to the sinus node or its artery, particularly during Fontan procedure or atrial switch operations (Senning and Mustard), may occur and result in persistent sinus bradycardia. If necessary, patients are treated with atrial or ventricular pacing, or chronotropic agents. Atrial and

ventricular pacing wires are usually placed at the time of open heart procedures and are left postoperatively until the desired heart rate and AV synchrony are returned and maintained.

- (b) Extreme sinus tachycardia is treated by eliminating causes (e.g., pain, anemia, fever, volume depletion, chronotropic agents). Administration of catecholamines should be minimized, as excessive tachycardia increases myocardial oxygen consumption. Furthermore, tachycardia shortens the diastolic period and consequently reduces coronary blood flow.
 - (c) Treatments of other arrhythmias are described in a section to follow.
- (6) Revision of surgical repair is occasionally indicated when an inadequate repair (such as a large residual L-R shunt or significant residual COA) is the cause of low cardiac output. Echo and, if necessary, cardiac catheterization may reveal a residual defect and its significance.
 - (7) Pulmonary hypertensive crisis is characterized by an acute rise in PA pressure followed by a reduction in cardiac output and a fall in arterial oxygen saturation. It occurs in neonates and infants who had CHDs with pulmonary hypertension (e.g., complete endocardial cushion defect [ECD], persistent truncus arteriosus), often after vigorous suctioning of the endotracheal tube. It is difficult to treat and may be fatal; prevention is critically important (see “General care” earlier in this chapter). Treatment includes sedation, paralysis, supplemental oxygen, and inhaled nitric oxide.
 - (8) Inadequate ventilation secondary to hemothorax, pleural effusion, or pneumothorax should be searched for and if necessary treated, such as with replacement of chest tube or even return to the operation room to manage possible hemorrhage.
- b. Hypotension and hypertension
 - (1) Hypotension due to low intravascular volume, recognized by low RA (central venous) and LA pressure, is treated as follows:
 - (a) Volume expanders or PRBCs are given as an IV bolus (initially 5-10 mL/kg, up to 20 mL/kg). As transfused citrated blood binds ionized calcium, replacement of calcium is necessary in maintaining BP and cardiac output.
 - (b) Inotropic agents are used if volume expansion fails to raise BP.
 - (c) Vasopressin (IV drip at 0.0003-0.01 U/kg/min) may be considered in patients with adequate myocardial function but with severe vasodilatory hypotension.
 - (2) Severe hypertension is treated with vasodilators (see “Low cardiac output syndrome” earlier in this chapter).
 - c. Rhythm disorders: Sinus rhythm and maintenance of AV synchrony are optimal. Junctional rhythm may reduce cardiac output by 10% to 15%. In addition to the specific treatment for arrhythmias, possible

causes should be investigated and corrected (e.g., oxygenation status, acid-base status, electrolyte imbalance, arrhythmogenic medications). If the patient is hemodynamically unstable, defibrillation or synchronized cardioversion should not be delayed.

- (1) Infrequent and isolated PACs or PVCs are followed without intervention.
- (2) Paroxysmal SVT (AV node and accessory pathway re-entry tachycardia) is treated with the drug of choice, adenosine (rapid IV bolus of 0.1 mg/kg/dose followed by rapid saline flush; if unsuccessful subsequent doses can be increased to 0.2 mg/kg). Intermittent episodes of SVT are treated with IV amiodarone (loading dose: 5-10 mg/kg over 20-60 minutes, followed by IV drip at a rate of 5-15 mcg/kg/min or IV boluses of 2.5 mg/kg every 6 hours). Persistent SVT may also be treated with overdrive suppression or synchronized cardioversion. In more resistant cases, other medications such as IV β -receptor blockers, verapamil, procainamide, and digoxin may be used with caution (taking into account myocardial function, BP stability, ventricular preexcitation, etc.). Oral β -receptor blockers, flecainide, or sotalol can be used in more chronic and stable patients.
- (3) Other SVTs (multifocal atrial tachycardia or ectopic atrial tachycardia) are treated by ventricular rate control with medications such as amiodarone, β -receptor blockers, calcium channel blockers, or digoxin.
- (4) Atrial flutter is treated with overdrive atrial pacing (through esophageal or intraoperatively placed temporary atrial leads) or synchronized cardioversion. Procainamide (loading dose: 2-6 mg/kg, maximum dose 100 mg/dose followed by IV continuous drip at 20-80 mcg/kg/min, maximum 2 g/day) and/or digoxin is the pharmacologic approach for this condition.
- (5) Atrial fibrillation is a rare condition in the acute postoperative pediatric cardiac population; nevertheless, it is treated with amiodarone, sotalol, or flecainide (in stable patients) or cardioversion (in hemodynamically compromised patients). If unsuccessful, ventricular rate control is the management of choice.
- (6) Postoperative junctional ectopic tachycardia (JET), the most common significant postoperative tachycardia, is discussed in detail in Chapter 29.
- (7) Frequent PVCs, if hemodynamically significant, are managed with avoidance of arrhythmogenic drugs, optimizing hemodynamic status, or correction of electrolyte imbalance (especially magnesium), hypoxia, and acidemia, and are suppressed with lidocaine (IV bolus 1 mg/kg followed by continuous drip at 20-50 mcg/kg/min).
- (8) Monomorphic VT with adequate perfusion is treated with amiodarone (loading dose: 5-10 mg/kg over 20 minutes, followed by IV drip at a rate of 5-15 mcg/kg/min or IV boluses of 2.5 mg/kg

every 6 hours), lidocaine (IV bolus of 1 mg/kg, followed by IV drip at 20-50 mcg/kg/min), procainamide (loading dose: 2-6 mg/kg, maximum dose 100 mg/dose, followed by IV continuous drip at 20-80 mcg/kg/min, maximum 2 g/day), esmolol (loading dose of 100-500 mcg/kg IV over one min followed by 50-500 mcg/kg/min continuous drip), or electrical cardioversion.

- (9) Torsades de pointes (uncommon variant of polymorphic VT), which occurs mostly in the setting of prolonged QT, requires a special approach. Amiodarone and procainamide may have a disastrous effect on this type of VT with further prolongation of the QT. Torsades often responds to IV magnesium sulfate (25-50 mg/kg, maximum dose 2 g), even when the magnesium level is normal. Esmolol and lidocaine may also be effective.
 - (10) Postoperative advanced second- or third-degree heart block is treated by temporary pacing and/or isoproterenol (IV drip at 0.05-2 mcg/kg/min). Permanent pacemaker implantation may be indicated if advanced AV block persists at least 7 days after the surgery.
4. Renal system: Anuria or oliguria (below 1 mL/kg/hr) and evidence of solute accumulation (serum K⁺ above 5 mEq/L, BUN above 40 mg/dL, creatinine above 1 mg/dL) indicate acute renal failure. Acute reduction of cardiac output is the most common cause of renal failure. Initial treatment is directed at improving cardiac output and inducing diuresis.
 - a. Preload and afterload should be optimized.
 - b. Furosemide, 0.5-2 mg/kg/dose every 6 to 12 hours IV or as a continuous IV drip at 0.05-0.4 mg/kg/hr, is given if the patient is oliguric.
 - c. If serum K⁺ rises above 6.0 mEq/L, calcium chloride (10 mg/kg/dose, slow central IV push), bicarbonate (1 mEq/kg/dose IV), D₂₅W (2 mL/kg IV; 0.5 g glucose/kg) plus regular insulin (0.1 U/kg IV) solution, and sodium polystyrene sulfonate (Kayexalate; 1 g/kg PR or NG) are used.
 - d. Peritoneal dialysis may be necessary if the above measures are ineffective. Indications for peritoneal dialysis include hypervolemia, azotemia (BUN over 150 mg/dL or lower if rising rapidly), life-threatening hyperkalemia, intractable metabolic acidosis, neurologic complications (secondary to uremia or electrolyte imbalance), calcium-phosphate imbalance, pulmonary compromise, or fluid restrictions limiting caloric intake.
 5. Metabolic system
 - a. Abnormalities of electrolytes and acid-base balance:
 - (1) Metabolic acidosis is treated if the base deficit is >5 mEq/L. Total extracellular base deficit = base deficit (mEq/L) × 0.3 × BW (kg). The dosage of sodium bicarbonate is half the total extracellular base deficit.
 - (2) Lactic acidemia may be caused by low cardiac output syndrome and ensuing poor cerebral and intestinal tissue perfusion. Treatment is directed at improvement of cardiac output.

- (3) Mild hyponatremia does not require treatment except for fluid restriction and diuresis. Serum $\text{Na}^+ < 125$ mEq/L requires treatment to elevate sodium levels.
 - (4) Hypernatremia with the serum $\text{Na}^+ > 155$ mEq/L requires treatment with sodium restriction and liberalization of fluids.
 - (5) Hypocalcemia may cause hypotension secondary to decreased myocardial function. It should be followed closely, especially in neonates and patients with DiGeorge syndrome. Ionized calcium level below 1.2 mEq/L should be treated. Central line administration is the ideal route of IV calcium, as extravasation will lead to tissue necrosis.
 - (6) Hypomagnesemia may lead to arrhythmia and subsequently to low cardiac output. A magnesium level of more than 0.7 mmol/L (1.4 mEq/L) is desirable.
- b. Postoperative hypoglycemia (below 5 mmol/L or 90 mg/dL) or hyperglycemia (above 7.8 mmol/L or 140 mg/dL) has been associated with increased mortality and morbidity. It seems prudent to avoid these conditions. Hypoglycemia is managed with bolus of dextrose or administration of higher concentrated glucose in water. Hyperglycemia is treated with restriction of glucose and/or infusion of insulin.
 - c. Postoperative hypothermia could interfere with hemostasis and exacerbate coagulopathy necessitating gradual rewarming to control hemorrhage. Shivering should be avoided as it increases the oxygen consumption. However, management of junctional ectopic tachycardia may include core temperature cooling. Unlike hypothermia, treatment of postoperative fever (above 38.5°C) is more urgent. Low cardiac output syndrome is one of the causes of postoperative hyperthermia so that management of postoperative fever not only includes antipyretics or cooling, but also optimizing cardiac output with afterload reduction.
6. Gastrointestinal system: Adequate caloric intake (120-150 kcal/kg/day) is essential in infants recovering from congenital cardiac surgery. Enteral feeding is individualized. When stable hemodynamically, several hours after extubation, oral feeding can be started with clear liquids (e.g., oral rehydration solutions). It is then advanced to an appropriate formula. Nasogastric tube feeding should be used in infants who are too weak to suck. Children with prolonged intubation require gavage feeding or total parenteral nutrition. Gastric protection is achieved with H_2 -receptor blockade (e.g., ranitidine, 1 mg/kg/dose IV every 6 to 8 hours) or protein pump inhibitors (e.g., esomeprazole, 0.5-1 mg/kg/dose IV every 24 hours, maximum pediatric dose 20 mg/day). The ranitidine dose needs to be adjusted in patients with renal failure or alternatively protein pump inhibitors could be used. Enterally fed patients should be examined frequently for any signs of intestinal dysfunction. Evidence of abdominal distention, absence of peristalsis, hyperperistalsis, or hematochezia is sought routinely. If one of these develops, enteral feeding is

discontinued, nasogastric suction is applied, and parenteral nutrition is considered. GI dysfunction may be caused by LCOS, acute pancreatitis, hepatic or intestinal necrosis, ileus, and others.

7. Hematologic system: Different thresholds are established for transfusion of PRBCs, fresh frozen plasma, or platelets at different institutions. Transfusion of blood products depends on hemodynamic status and coagulation status of individual patients.
 - a. Maintain adequate hemoglobin (Hgb) and a desirable filling pressure (e.g., LA pressure 10-15 mm Hg) by infusion of PRBCs or albumin, depending on the patient's Hgb or hematocrit (Hct). Patients with cyanotic congenital heart disease or myocardial dysfunction are given PRBCs to maintain Hct above 40%.
 - b. Coagulation abnormalities may result from inadequate heparin neutralization (causing prolongation of aPTT), thrombocytopenia (below 50,000 platelets/mm³), or disseminated intravascular coagulation (DIC; secondary to sepsis, low cardiac output, acidosis, hypoxia, or tissue necrosis or as a reaction to blood transfusion).
 - (1) Unneutralized heparin is corrected by administration of additional protamine.
 - (2) Thrombocytopenia is treated with slow infusion of platelet concentrates with an infusion pump, given over 20 to 30 min; rapid infusion may cause pulmonary hypertension and RV failure.
 - (3) DIC (characterized by hemorrhage, tissue necrosis, hemolytic anemia, positive D-dimer test, low platelets and serum fibrinogen, and prolonged PT and aPTT) is managed by prompt and vigorous treatment of the underlying cause. Management may include transfusion of platelets, cryoprecipitates, and/or fresh-frozen plasma as well as administration of heparin.
 - c. Excessive postoperative bleeding occurs more frequently in severely cyanotic patients, polycythemic patients, and patients who had a reoperation. Necessity to infuse more than 10-15 mL/kg of volume requires investigation for excessive blood loss and for a possible surgical exploration. Surgical exploration is indicated (1) if the chest tube drainage in the absence of clotting abnormalities exceeds 3 mL/kg/hr for 3 hours or (2) if there is a sudden marked increase in chest tube drainage of 5 mL/kg/hr in any 1 hour.
 - d. Long-term anticoagulation with aspirin or warfarin is indicated in selected patients. Patients with cavopulmonary anastomosis (e.g., Glenn or Fontan procedure) or systemic-to-pulmonary shunts (e.g., modified Blalock-Taussig shunt) are bridged to oral anticoagulation by continuous heparin drip and its dose is adjusted for aPTT of 60-85 seconds. Aspirin (3-5 mg/kg PO once daily) is started when chest is closed, all major intracardiac lines are removed, and patients are hemodynamically stable and have adequate platelet count without evidence of active bleeding. Alternatively or additionally, warfarin is given if the patient is in a hypercoagulable state (e.g., factor V Leiden

mutation, protein S or C deficiency). Patients with mechanical valve prosthesis will require warfarin; the dose is adjusted to maintain adequate anticoagulation (INR 2.5-3.5). While patients are maintained on aspirin, cyclooxygenase (COX)-2 inhibitors (e.g., ibuprofen, naproxen) should be avoided as they inhibit the antiplatelet effect of aspirin.

8. Neurologic system: The incidence of central nervous system anomalies including brain dysmorphology or neurobehavioral abnormalities is increased in patients with congenital cardiac defects. These may be multifactorial, isolated findings, or in association with particular genetic defects. In addition, pre- and perioperative neurologic events complicate establishing the accurate cause of the neurologic insult.

a. Localized neurologic defects such as hemiplegia and visual field defects are abnormal and may be due to air or particulate emboli.

b. Seizures may be caused by hypoxia, metabolic abnormalities, infections, cerebral edema, embolism or hemorrhage, or decreased cerebral perfusion. Early postoperative clinical seizures occur at an incidence rate of 3-6%; however, EEG and video monitoring may reveal an incidence of 20% of subclinical seizures. EEG documented seizures have been associated with worse neurodevelopmental outcome. Management of seizures includes the following:

(1) Determine arterial blood gases, serum glucose, calcium, electrolytes, cardiac output, and temperature. Correct any abnormalities.

(2) Anticonvulsant therapy

(a) Lorazepam, 0.05-0.1 mg/kg/dose IV over 2 to 5 min (maximum single dose 2 mg; may cause respiratory depression).

(b) Fosphenytoin, 15-20 mg phenytoin equivalent (PE)/kg IV (maximum infusion rate of 150 mg PE/min due to risk of hypotension), followed by a maintenance dose of 5 mg PE/kg/day IV or IM. Therapeutic levels are 10-20 mg/L (free and bound phenytoin) or 1-2 mg/L (free phenytoin). Fosphenytoin causes less hypotension than traditional phenytoin; however, both medications are contraindicated in patients with heart block or sinus bradycardia.

(c) Phenobarbital, 10-20 mg/kg IV over 5-10 minutes. The full effect may take several hours. Phenobarbital maintenance dose is 5 mg/kg/day given in 1 or 2 daily doses. Therapeutic level is 10-40 mg/L. Side effects of phenobarbital include myocardial depression with hypotension, particularly after large and rapid infusion.

c. Choreiform movement and grossly inadequate behavior are major neurologic complications. Pharmacologic control is difficult. These complications usually but not always clear without demonstrable sequelae.

Selected Postoperative Complications

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Selected postoperative complications are discussed briefly in this chapter. Problems that occur in the immediate postoperative period, such as low cardiac output state, minor rhythm disorders, blood pressure abnormalities, and renal, metabolic, and hematologic abnormalities, are discussed in Chapter 27. Postoperative complications that occur frequently with certain types of cardiac defects are discussed under those specific conditions.

A. Pleural Effusion

A small amount of fluid is present in the pleural cavity. The reabsorption of this pleural fluid is mainly through the venous system and to some degree through the lymphatic system. Any increase in capillary hydrostatic pressure as a result of disrupted systemic venous hemodynamics (e.g., Fontan surgery, right ventricular failure) may result in accumulation of transudates in the pleural cavity. Trauma to the lymphatic system as is caused by cutting large tributaries of the thoracic duct causes buildup of chyle in the pleural space. Both conditions create a management problem.

Duration of *persistent pleural effusion*, as a result of increased systemic venous pressure which is common after Fontan operation, may be shortened by intraoperative creation of baffle fenestration. Symptoms may include fever, tachycardia, tachypnea, increased work of breathing, and, in severe cases, respiratory failure. Diagnosis is usually made by chest radiography (frontal, lateral, and decubitus films). Thoracentesis (with ultrasonographic guidance) may be necessary for determination of etiology and/or for treatment. Transudates can be differentiated by amount of protein (less than 3 g/100 mL) and lactate dehydrogenase (LDH) (less than 200 IU/L) from exudates (protein of more than 3 g/100 mL and LDH of more than 200 IU/L) which are caused by increased capillary permeability and may be a sign of infection. In addition, transudates have fewer leukocytes (less than 10,000/mm³) and have a serous appearance compared to exudates, which are cloudy and have significantly more leukocytes (more than 50,000/mm³). Furthermore, fluid-to-serum ratios of LDH (more than 0.6) and protein (more than 0.5) are further clues to the exudative nature of the fluid.

A small amount of pleural effusion can be tolerated well. It usually responds to medical management with diuresis, afterload reduction, and inotropic support. However, significant amounts of pleural effusion will cause cardiorespiratory compromise and will require more aggressive management strategies, including chest tube drainage, pleurodesis with a sclerosing agent (e.g., talc), or even Fontan revision. When the drainage is large, appropriate replacement of fluid, electrolytes, and protein is essential.

Chylothorax, an accumulation of chyle in the pleural cavity, may be caused by trauma to peritracheal lymphatics or transmission of increased systemic venous pressure to the thoracic duct, or a combination of both. It may be seen after surgery (up to about 6% of cases) such as COA repair, B-T shunt, or cavopulmonary anastomosis (e.g., Glenn or Fontan operation), or, rarely, after ligation of PDA. Occasionally, chylothorax occurs in combination with chylopericardium.

Chyle may or may not have a creamy appearance, depending on the nutritional status of the patient (consumption of fat results in creamy appearance), but a triglyceride level above 110 mg/dL is highly probable for the diagnosis whereas a triglyceride concentration of less than 50 mg/dL almost rules out chylothorax. The fluid is usually sterile and is abundant of lymphocytes (2000-20,000/mm³).

Treatment, apart from medical management described previously, is directed at drainage of chylothorax (chest tube placement) and reducing the flow of lymph (by limiting physical activity to reduce lymph flow from the extremities).

1. In most cases, chest tube drainage is all that is necessary. If chylothorax develops after chest tube removal, needle aspiration every 3 to 4 days usually constitutes adequate treatment. The drainage slows or stops within 7 days in most cases.
2. Careful attention to the nutrition of the patient is important. Either parenteral hyperalimentation or a diet with medium-chain triglyceride (MCT) as the fat source is called for. As MCT oil does not contribute in chylomicron formation, it is absorbed by the portal system and not by the lymphatic system. Serum albumin should be followed closely and replaced if necessary.
3. In some case reports, continuous IV octreotide (0.5-10 mcg/kg/hr), a somatostatin analog, has been used effectively.
4. If the drainage persists, surgical intervention may be considered because continuous loss of chyle results in lymphocyte depletion and subsequent immunocompromise. Indications for the intervention may include (1) average daily loss above 1000 mL, or, in children, 100 mL/year of age for 5 days, (2) the chyle flow not slowing after 2 weeks, or (3) imminent nutritional complications.
5. Thoracic duct ligation with or without chemical pleurodesis has been used successfully. During pleurodesis, the introduced chemicals cause inflammation between the parietal and visceral pleura. This reaction causes adhesions between the layers and prevents further fluid accumulation. The procedure may be painful and cause fever and nausea.

B. Paralysis of the Diaphragm

Paralysis or paresis of a hemidiaphragm occurs in about 0.5% to 2% of patients after thoracic surgery, though the incidence may be as high as 10% in young children. It is the result of damage to the phrenic nerve. It may occur after COA repair, PDA ligation, B-T shunt, or open heart surgery and may be due to nerve transection, blunt trauma, stretching during retraction, electrocautery, or hypothermic injury. Infants are more vulnerable to respiratory distress due to their greater dependence on the diaphragm for respiration.

The diagnosis should be suspected if there is persistent unexplained tachypnea, respiratory distress, hypoxia and/or hypercapnia, atelectasis, inability to wean from the ventilator, or persistent elevation of a hemidiaphragm on serial chest radiographs. Fluoroscopy or sonogram that reveals paradoxical motion of the hemidiaphragms is diagnostic if it is done during spontaneous breathing. When paralysis is not caused by transection, return of function usually occurs in 2 weeks to 6 months. In 20% of the cases the paralysis is permanent.

Management ranges from conservative to surgical intervention.

1. Some investigators recommend ventilator support only for the initial 2 to 6 weeks.
2. Continuous positive airway pressure (CPAP) may be useful in management as well as in identifying patients who may benefit from plication.
3. If respiratory insufficiency persists, surgical plication should be considered. Plication of the diaphragm usually is not necessary as long as the patient can be extubated without developing respiratory insufficiency.

C. Postpericardiotomy Syndrome

Postpericardiotomy syndrome (PPS), a febrile illness with pericardial and pleural inflammatory reactions, develops after surgery involving pericardiotomy. This occurs in about 25% to 30% of patients who undergo pericardiotomy. The etiology remains speculative. Though questioned in more recent studies, an autoimmune response to cardiac antibodies in association with a recent or remote viral infection was postulated in the 1970s. Studied patients who developed PPS had a high titer of antiheart antibodies along with high antibody titers against adenovirus, coxsackievirus B1-6, and cytomegalovirus.

Onset is a few weeks to a few months (median 4 weeks) after pericardiotomy. PPS is characterized by fever, chest pain, irritability, malaise, joint pain, decreased appetite, nausea, and vomiting. Chest pain, which may be severe, is caused by both pericarditis and pleuritis. It may be worse in supine position or with deep inspiration. It is rare in infants younger than 2 years of age. Physical examination may reveal pericardial and pleural friction rubs and hepatomegaly. Tachycardia, tachypnea, rising venous pressure, falling arterial pressure, and narrow pulse pressure with a paradoxical pulse are signs of cardiac tamponade. Blood laboratory findings include leukocytosis with left shift. Erythrocyte sedimentation rate (ESR)

and C-reactive protein (CRP) are usually elevated. Chest radiography shows enlarged cardiac silhouette and pleural effusion. ECG shows persistent ST-segment elevation and flat or inverted T waves in the limb and left precordial leads. Echo is a reliable test in confirming the presence and amount of pericardial effusion and in evaluating evidence of cardiac tamponade. Although the disease is self-limited, its duration is highly variable; the median duration is 2 to 3 weeks. About 20% of patients have recurrences.

Bed rest is all that is needed for a mild case. A nonsteroidal antiinflammatory agent such as oral aspirin (80-100 mg/kg/day divided in 3 or 4 doses) or ibuprofen (20-40 mg/kg/day divided in 3 or 4 doses) is effective in most cases. In severe cases, corticosteroids (prednisone, 2 mg/kg/day up to 60 mg/day) tapered over 3 to 4 weeks may be indicated if the diagnosis is secure and infection has been ruled out. Emergency pericardiocentesis or creation of pericardial window may be required if signs of cardiac tamponade are present. Diuretics may be used for pleural effusion.

D. Postcoarctectomy Hypertension

Paradoxical hypertension following repair of coarctation of the aorta is quite common, particularly in older children. This condition is usually biphasic with mostly systolic hypertension developing within 24 to 48 hours of the procedure, followed by a more delayed phase. The mechanism is believed to be multifactorial, including intraoperative stimulation of sympathetic nerve fibers, postoperative altered baroreceptor activity, and derangement of the renin-angiotensin system. The first phase of hypertension is believed to be the result of increased catecholamine levels and altered baroreceptor response. Elevated levels of renin and angiotensin are believed to be responsible for the later phase hypertension which is more pronounced in diastole.

Systemic hypertension needs to be treated promptly, as this could increase the risk of postoperative hemorrhage. In addition to pain management and sedation, short-acting intravenous β -receptor blocker administration (e.g., esmolol, loading dose of 100-500 mcg/kg IV over one minute followed by 50-500 mcg/kg/min continuous drip) can be used to control the first phase of postcoarctectomy hypertension. Other medications that have been used successfully include longer-acting β -receptor blockers (e.g., propranolol, nadolol), combined α - and β -receptor blockers (e.g., labetalol), and vasodilators (nitroprusside, hydralazine). Long-term management of paradoxical hypertension is achieved with angiotensin-converting enzyme inhibitors (e.g., enalapril, captopril) or angiotensin II receptor antagonists (e.g., losartan).

Postcoarctectomy syndrome is a well-described but rare complication of repair of COA. Occurring in up to 5% to 10% of older children, it is characterized by severe, intermittent abdominal pain beginning 2 to 4 days after surgery with accompanying fever, leukocytosis, and vomiting. In severe cases ascites, ileus, melena, ischemic bowel, and even death were reported. Persistent paradoxical hypertension may be present. Abdominal findings are believed to be caused by acute inflammatory changes in

mesenteric arteries resulting from sudden increase in pulsatile pressures in arteries distal to the coarctation.

Because of mesenteric arteritis feeding of solid foods is delayed; some centers advocate NPO status for the first 48 hours following the repair. Treatment includes bowel decompression and treatment of the accompanying hypertension.

E. Protein-Losing Enteropathy

Protein-losing enteropathy (PLE) is a condition characterized by excessive loss of plasma protein through the intestinal mucosa. Although it can be a primary gastrointestinal disorder with intestinal lymphangiectasia and associated peripheral edema, PLE occurs most frequently as a complication of Fontan procedure. It is believed to be caused by chronically elevated central venous pressure secondary to unfavorable PA anatomy, increased PVR, decreased cardiac output, or loss of electrical AV synchrony. PLE in association with Fontan-type surgery has a cumulative 10-year occurrence risk of 13% and a poor 5-year survival rate of about 50%.

Children may present, a few weeks, months, or even years after the surgery, with symptoms of anasarca, abdominal pain and distension, diarrhea, emesis, and poor weight gain. Patients may be tachycardic if sinus node function is preserved. Tachypnea may be a clue to concurrent pleural effusion. Hepatomegaly is seen frequently. Signs of fluid retention including ascites and anasarca may be found on examination.

Serum albumin, immunoglobulins, and total protein are decreased. In addition, α 1-antitrypsin 24-hour fecal clearance and α 1-antitrypsin random fecal concentration are increased. Technetium-99m dextran scintigraphy may be performed to assess the extent or possibly the location of intestinal protein loss. Electrolyte imbalance is seen which may be iatrogenic secondary to diuretic therapy. ECG and Holter monitoring need to be obtained to rule out any arrhythmia such as sinus node dysfunction. Chest radiography may reveal cardiomegaly and/or pleural effusion. Echo is performed to evaluate ventricular function or Fontan baffle obstruction. Cardiac catheterization may be needed as a diagnostic but also as a therapeutic tool.

Treatment includes the following:

1. High-protein, low-fat, high-MCT diet
2. Diuretics (furosemide, spironolactone)
3. ACE inhibitors (enalapril)
4. Phosphodiesterase type 5 inhibitors (sildenafil)
5. Intravenous albumin
6. Subcutaneous low molecular weight heparin (enoxaparin, 0.5-1.5 mg/kg/dose SC every 12 to 24 hours; to achieve target anti-factor Xa levels of 0.5-1 units/mL in a sample taken 4 to 6 hours after SC injection)
7. Corticosteroids (budesonide, 6 mg for children younger than 4 years, 9 mg for children older than 4 years; dose should be weaned after normalization of albumin [3 mg/dL] to lifelong 3 mg every other day)
8. Trial of octreotide (continuous IV drip 0.5-10 mcg/kg/hour)

More invasive management apart from interventional cardiac catheterization may include pacemaker insertion, repair of residual defects (e.g., repair of AV valve, repair of residual COA), Fontan revision, or cardiac transplantation.

F. Junctional Ectopic Tachycardia

Postoperative junctional ectopic tachycardia (JET) occurs in 5% to 10% of pediatric postoperative patients, most frequently following surgeries adjacent to the AV node (e.g., VSD, TOF, ECD repair, Fontan procedure), as well as in patients with prolonged aortic cross-clamp and cardiopulmonary bypass times. Postoperative JET usually occurs within hours after cardiac surgery and may last for several days. Though it is self-limited, it is a serious and life-threatening arrhythmia due to its occurrence in a very vulnerable phase of a patient's postoperative course. It is characterized by tachycardia with a ventricular rate usually in excess of 180 beats per minute (faster than atrial rate), atrioventricular (AV) dissociation (unlike re-entrant SVT), and capture beats (occasional antegrade conduction of a normal sinus beat).

Driven by an automatic focus within the proximity of the AV node or bundle of His, JET does not respond to strategies such as electrical or pharmacologic cardioversion. Tachycardia and loss of AV synchrony are responsible for a decrease in cardiac output especially in an already hemodynamically compromised patient. Treatment is aimed at correcting tachycardia and restoring AV synchrony as well as optimizing cardiac output.

1. Measures to maximize cardiac output include the following:
 - a. Treatment of anemia.
 - b. Treatment of acidosis.
 - c. Inotropic, lusitropic, and vasodilatory support with milrinone without the undesired arrhythmogenic effect.
 - d. Measures to decrease oxygen consumption (e.g., pain control, sedation, and, if necessary, paralysis).
2. Attempts to restore AV synchrony include:
 - a. Correction of electrolyte imbalance (Mg^{2+} , Ca^{2+} , and K^+).
 - b. Attempting atrial pacing at a rate higher than the JET rate to achieve AV synchrony, once the ventricular rate is less than 200 BPM.
3. Attempts to control the ventricular rate, though challenging, may include the following strategies and/or antiarrhythmic medications:
 - a. Fever control.
 - b. Lowering the infusion rate of catecholamines (proarrhythmogenic).
 - c. Antiarrhythmics:
 - (1) Intravenous amiodarone (loading dose: 5-10 mg/kg over 20-60 minutes, followed by IV drip at a rate of 5-15 mcg/kg/min or IV boluses of 2.5 mg/kg every 6 hours).
 - (2) Combination of intravenous procainamide (loading dose: 2-6 mg/kg, maximum dose 100 mg/dose, followed by IV drip at 20-80 mcg/kg/min, maximum 2 g/day) and hypothermia.

- (3) Intravenous esmolol (loading dose: 100-500 mcg/kg IV over one minute, followed by IV drip at 50-500 mcg/kg/min).
 - d. Induced hypothermia (34-36°C) using cooling blanket or intravenous cold saline infusions.
4. If the above efforts to control JET fail and the patient continues to deteriorate, extracorporeal life support (ECLS) may need to be initiated.

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APPENDICES

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Appendix A

Miscellaneous

TABLE A-1

RECURRENCE RISKS GIVEN ONE SIBLING WHO HAS A CARDIOVASCULAR ANOMALY

ANOMALY	SUGGESTED RISK (%)
Ventricular septal defect	3.0
Patent ductus arteriosus	3.0
Atrial septal defect	2.5
Tetralogy of Fallot	2.5
Pulmonary stenosis	2.0
Coarctation of the aorta	2.0
Aortic stenosis	2.0
Transposition of the great arteries	1.5
Atrioventricular canal (complete endocardial cushion defect)	2.0
Endocardial fibroelastosis	4.0
Tricuspid atresia	1.0
Ebstein anomaly	1.0
Persistent truncus arteriosus	1.0
Pulmonary atresia	1.0
Hypoplastic left heart syndrome	2.0

Modified from Nora JJ, Nora AH: The evaluation of specific genetic and environmental counseling in congenital heart diseases, *Circulation* 57:205-213, 1978.

TABLE A-2

AFFECTED OFFSPRING GIVEN ONE PARENT WITH A CONGENITAL HEART DEFECT

DEFECT	MOTHER AFFECTED (%)	FATHER AFFECTED (%)
Aortic stenosis	13.0-18.0	3.0
Atrial septal defect	4.0-4.5	1.5
Atrioventricular canal (complete endocardial cushion defect)	14.0	1.0
Coarctation of the aorta	4.0	2.0
Patent ductus arteriosus	3.5-4.0	2.5
Pulmonary stenosis	4.0-6.5	2.0
Tetralogy of Fallot	6.0-10.0	1.5
Ventricular septal defect	6.0	2.0

From Nora JJ, Nora AH: Maternal transmission of congenital heart disease: New recurrence risk figures and the questions of cytoplasmic inheritance and vulnerability to teratogens, *Am J Cardiol* 59:459-463, 1987.

TABLE A-3
NEW YORK HEART ASSOCIATION FUNCTIONAL CLASSIFICATION

CLASS	IMPAIRMENT
I	The patient has the disease, but the condition is asymptomatic.
II	The patient experiences symptoms with moderate activity.
III	The patient has symptoms with mild activity.
IV	The patient's condition is symptomatic at rest.

This is a classification of functional impairment in exercise capacity based on symptoms of dyspnea and fatigue. It is simple and useful in the evaluation of cardiac patients.

TABLE A-4
SUMMARY OF ANTIARRHYTHMIC AGENTS

CLASS	MECHANISM OF ACTION	EXAMPLES	REMARKS
I	Sodium channel blockers Delays phase 0 of the action potential and slows conduction velocity in the tissue		Has a significant proarrhythmic effect
IA	Slows the rate of rise of phase 0 and prolongs the refractory period	Quinidine Procainamide	Major effect on QTc and QRS prolongation
IB	Minimal effect on phase 0 and refractory period	Lidocaine Mexiletine	Least proarrhythmic among Class I agents
IC	Marked depression in conduction velocity with minimal effects on refractoriness	Flecainide Propafenone	Major effect on PR and QRS duration
II	β -blockers	Propranolol ($\beta_1 + \beta_2$) Atenolol (β_1) Nadolol ($\beta_1 + \beta_2$) Esmolol (β_1)	Minor effects on ECG
III	K-channel blockers Delays repolarization	Amiodarone Sotalol Dofetilide Ibutilide	Has a significant proarrhythmic effect Major effect on QT prolongation
IV	Ca-channel blockers (slows inward Ca^{2+} current) Slows conduction velocity and increases refractoriness in the AV node	Verapamil Diltiazem	Minor effects on ECG

AV, atrioventricular; WCG, electrocardiogram.

TABLE A-5

EFFECTS OF ANTIARRHYTHMIC AGENTS ON THE ECG

		PR	QRS	QT
CLASS I				
IA	Quinidine	±	↑↑	↑↑↑
	Procainamide	±	↑	↑↑
IB	Lidocaine	±	±	±
	Mixiletine	±	±	±
IC	Flecainide	↑↑	↑↑	↑
	Propafenone	↑↑	↑↑	±
CLASS III	Amiodarone	Acu ±	Acu ±	Acu ±
		Chr ↑	Chr ↑	Chr ↑↑↑
	Sotalol	↑	±	↑↑↑
	Dofetilide	±	±	↑↑↑
	Ibutilide	±	±	↑↑↑

Acu, acute effect; Chr, chronic effect.

Modified from Fischbach PS: Pharmacology of antiarrhythmic agents. In Macdonald D II (ed.), Clinical Cardiac Electrophysiology in the Young, Springer, New York, 2010.

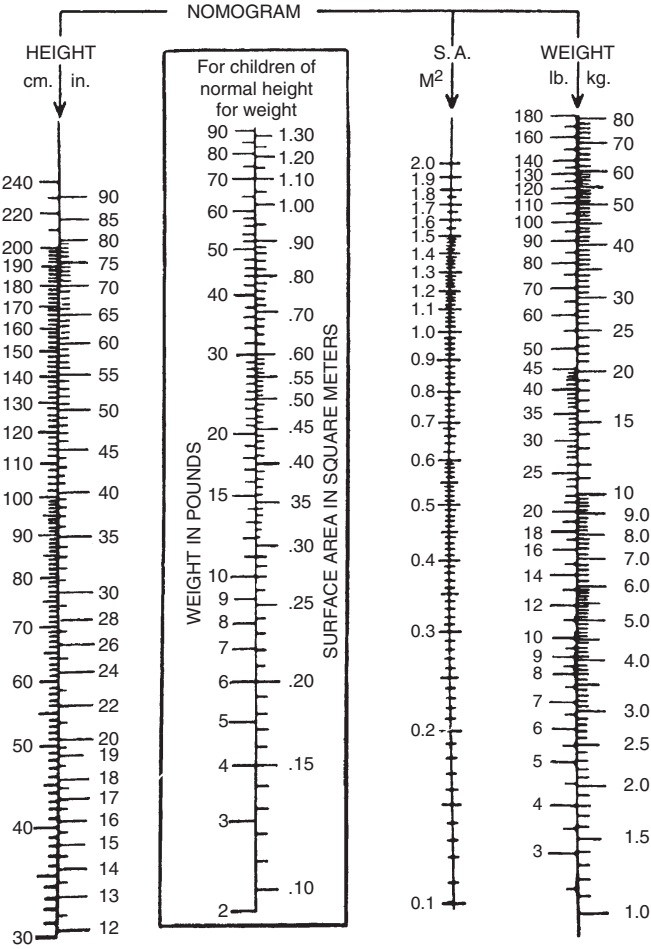


FIGURE A-1
Body surface area nomogram.

TABLE A-6

OXYGEN CONSUMPTION PER BODY SURFACE AREA*

AGE (YR)	Heart Rate (beats/min)												
	50	60	70	80	90	100	110	120	130	140	150	160	170
MALE PATIENTS													
3				155	159	163	167	171	175	178	182	186	190
4			149	152	156	160	163	168	171	175	179	182	186
6		141	144	148	151	155	159	162	167	171	174	178	181
8		136	141	145	148	152	156	159	163	167	171	175	178
10	130	134	139	142	146	149	153	157	160	165	169	172	176
12	128	132	136	140	144	147	151	155	158	162	167	170	174
14	127	130	134	137	142	146	149	153	157	160	165	169	172
16	125	129	132	136	141	144	148	152	155	159	162	167	
18	124	127	131	135	139	143	147	150	154	157	161	166	
20	123	126	130	134	137	142	145	149	153	156	160	165	
25	120	124	127	131	135	139	143	147	150	154	157		
30	118	122	125	129	133	136	141	145	148	152	155		
35	116	120	124	127	131	135	139	143	147	150			
40	115	119	122	126	130	133	137	141	145	149			

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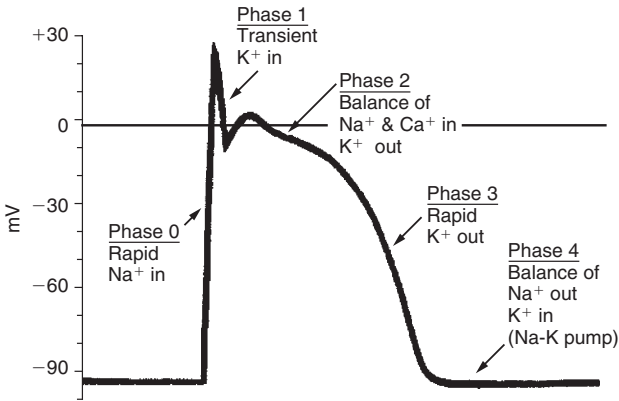
TABLE A-6

OXYGEN CONSUMPTION PER BODY SURFACE AREA (Continued)

AGE (YR)	Heart Rate (beats/min)												
	50	60	70	80	90	100	110	120	130	140	150	160	170
FEMALE PATIENTS													
3				150	153	157	161	165	169	172	176	180	183
4			141	145	149	152	156	159	163	168	171	175	179
6		130	134	137	142	146	149	153	156	160	165	168	172
8		125	129	133	136	141	144	148	152	155	159	163	167
10	118	122	125	129	133	136	141	144	148	152	155	159	163
12	115	119	122	126	130	133	137	141	145	149	152	156	160
14	112	116	120	123	127	131	134	133	143	146	150	153	157
16	109	114	118	121	125	128	132	136	140	144	148	151	
18	107	111	116	119	123	127	130	134	137	142	146	149	
20	106	109	114	118	121	125	128	132	136	140	144	148	
25	102	106	109	114	118	121	125	128	132	136	140		
30	99	103	106	110	115	118	122	125	129	133	136		
35	97	100	104	107	111	116	119	123	127	130			
50	94	98	102	105	109	112	117	121	124	128			

*In (mL/min)/m².

From LaFarge CG, Miettinen OS: The estimation of oxygen consumption, Cardiovasc Res 4:23, 1970.

**FIGURE A-2**

Action potential of human ventricular myocyte of subepicardial origin. **Phase 0** (rapid depolarization) is the result of sudden increase in membrane conductance to Na⁺ ion. **Phase 1** (early rapid repolarization) is due to transient outward K⁺ current. **Phase 2** (plateau) is maintained by the competition between outward current carried by K⁺ and Cl⁻ ions and inward current carried by Ca²⁺ ions. **Phase 3** (final rapid repolarization) is due to activation of repolarizing outward K⁺ current. **Phase 4** (the resting potential or diastolic depolarization) is due to the Na-K pump that maintains high K⁺ concentration and low intracellular Na⁺ concentration by pumping K⁺ inward and Na⁺ outward.

TABLE B-1

BP LEVELS FOR BOYS BY AGE AND HEIGHT PERCENTILE (NHBPEP*)

AGE	BP PERCENTILE	Systolic BP (mm Hg)								Diastolic BP (mm Hg)							
		Percentile of Height								Percentile of Height							
		5TH	10TH	25TH	50TH	75TH	90TH	95TH	5TH	10TH	25TH	50TH	75TH	90TH	95TH	5TH	95TH
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39		
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54		
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58		
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66		
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44		
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59		
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63		
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71		
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48		
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63		
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67		
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75		
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52		
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67		
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71		
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79		

5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89

Continued

TABLE B-1

BP LEVELS FOR BOYS BY AGE AND HEIGHT PERCENTILE (NHBPEP) (Continued)

AGE	BP PERCENTILE	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Percentile of Height							Percentile of Height						
		5TH	10TH	25TH	50TH	75TH	90TH	95TH	5TH	10TH	25TH	50TH	75TH	90TH	95TH
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92

15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

*National High Blood Pressure Education Program

From The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, Pediatrics 114:555-576, 2004.

TABLE B-2

BP LEVELS FOR GIRLS BY AGE AND HEIGHT PERCENTILE (NHBPEP*)

AGE	BP PERCENTILE	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Percentile of Height							Percentile of Height						
		5TH	10TH	25TH	50TH	75TH	90TH	95TH	5TH	10TH	25TH	50TH	75TH	90TH	95TH
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81

6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90

Continued

TABLE B-2

BP LEVELS FOR GIRLS BY AGE AND HEIGHT PERCENTILE (NHBPEP) (Continued)

AGE	BP PERCENTILE	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Percentile of Height							Percentile of Height						
		5TH	10TH	25TH	50TH	75TH	90TH	95TH	5TH	10TH	25TH	50TH	75TH	90TH	95TH
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

*National High Blood Pressure Education Program

From The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, Pediatrics 114:555-576, 2004.

TABLE B-3

**AUSCULTATORY BLOOD PRESSURE VALUES FOR BOYS 5 TO 17 YEARS OLD
(SAN ANTONIO CHILDREN'S BLOOD PRESSURE STUDY)**

AGE (YR)	Percentiles							
	5TH	10TH	25TH	MEAN	75TH	90TH	95TH	99TH*
SYSTOLIC PRESSURE								
5	78	81	87	92	98	103	106	112
6	81	84	89	95	100	105	108	114
7	82	85	90	96	102	107	110	116
8	83	86	92	97	103	108	111	117
9	85	88	93	99	104	109	113	118
10	86	89	95	100	106	111	114	120
11	88	91	97	102	108	113	116	122
12	91	94	99	105	111	116	119	125
13	94	97	102	108	113	118	122	127
14	96	99	105	110	116	121	122	130
15	99	102	107	113	118	124	127	132
16	100	103	108	114	120	125	128	134
17	100	103	109	114	120	125	128	134
DIASTOLIC PRESSURE (K5)								
5	34	37	43	49	55	60	63	70
6	38	41	47	53	59	64	67	73
7	40	44	49	55	61	66	70	76
8	42	45	50	56	62	68	71	77
9	42	45	51	57	63	68	71	77
10	42	45	51	57	63	68	71	77
11	42	45	51	57	63	68	71	77
12	42	45	50	56	62	68	71	77
13	42	45	51	56	62	68	71	77
14	42	45	51	57	63	68	71	77
15	43	46	51	57	63	69	72	78
16	45	48	53	59	65	71	74	80
17	47	51	56	62	68	73	77	83

*The 99th percentile values were added after publication.

Data presented in graphic form in Park MK, Menard SW, Yuan C: Comparison of blood pressure in children from three ethnic groups, Am J Cardiol 87:1305-1308, 2001.

TABLE B-4

AUSCULTATORY BLOOD PRESSURE VALUES FOR GIRLS 5 TO 17 YEARS OLD

(SAN ANTONIO CHILDREN'S BLOOD PRESSURE STUDY)

AGE (YR)	Percentiles							
	5TH	10TH	25TH	MEAN	75TH	90TH	95TH	99TH*
SYSTOLIC PRESSURE								
5	79	82	87	92	97	102	105	110
6	80	83	88	93	98	103	106	111
7	81	84	89	94	99	104	107	112
8	83	86	91	96	101	106	109	114
9	85	88	93	98	103	108	111	116
10	87	90	95	100	105	110	113	118
11	89	92	97	102	107	112	115	120
12	91	94	98	104	109	113	116	122
13	92	95	100	105	110	115	118	123
14	93	96	101	106	111	116	119	124
15	94	97	101	107	112	117	119	125
16	94	97	102	107	112	117	120	125
17	95	98	103	108	113	118	121	126
DIASTOLIC PRESSURE (K5)								
5	35	38	44	49	55	60	63	69
6	38	41	47	52	58	63	66	72
7	40	41	49	54	60	65	68	74
8	42	45	50	56	61	67	70	75
9	43	46	51	56	62	67	70	76
10	43	46	51	57	63	68	71	77
11	43	46	51	57	63	68	71	77
12	43	46	52	57	63	68	71	77
13	43	47	52	57	63	68	71	77
14	44	47	52	58	63	68	72	77
15	44	47	52	58	64	69	72	78
16	45	48	53	59	64	69	73	78
17	46	49	54	59	65	70	73	79

*The 99th percentile values were added after publication.

Data presented in graphic form in Park MK, Menard SW, Yuan C: Comparison of blood pressure in children from three ethnic groups, Am J Cardiol 87:1305-1308, 2001.

TABLE B-5

**DINAMAP (MODEL 8100) BLOOD PRESSURE VALUES FOR BOYS 5 TO 17 YEARS OLD
(SAN ANTONIO CHILDREN'S BLOOD PRESSURE STUDY)**

AGE (YR)	Percentiles							
	5TH	10TH	25TH	MEAN	75TH	90TH	95TH	99TH*
SYSTOLIC PRESSURE								
5	90	93	98	104	110	115	118	124
6	92	95	100	106	112	117	120	126
7	93	96	102	107	113	118	121	127
8	94	97	103	108	114	119	123	128
9	95	99	104	110	115	121	124	130
10	97	100	105	110	117	122	125	131
11	99	102	107	113	119	124	127	133
12	101	104	109	115	121	126	129	135
13	104	107	112	118	123	129	132	138
14	106	109	114	120	126	131	134	140
15	108	111	116	122	128	133	136	141
16	109	112	117	123	128	134	137	143
17	109	112	117	123	129	134	137	143
DIASTOLIC PRESSURE								
5	46	49	53	58	63	68	71	76
6	47	49	54	59	64	68	71	76
7	47	50	54	59	64	69	72	77
8	48	51	55	60	65	70	72	78
9	49	51	56	61	66	70	73	78
10	49	52	56	61	66	71	74	79
11	49	52	57	62	67	71	74	79
12	50	52	57	62	67	71	74	79
13	50	52	57	62	67	71	74	79
14	50	52	57	62	67	72	74	79
15	50	52	57	62	67	72	74	79
16	50	53	57	62	67	72	74	80
17	50	53	57	62	67	72	75	80

*The 99th percentile values were added after submission of the manuscript.

From Park MK, Menard SW, Schoolfield J: Oscillometric blood pressure standards for children, *Pediatr Cardiol* 2005 (in press).

TABLE B-6

DINAMAP (MODEL 8100) BLOOD PRESSURE VALUES FOR GIRLS 5 TO 17 YEARS OLD (SAN ANTONIO CHILDREN'S BLOOD PRESSURE STUDY)

AGE (YR)	Percentiles							
	5TH	10TH	25TH	MEAN	75TH	90TH	95TH	99TH*
SYSTOLIC PRESSURE								
5	90	93	98	103	109	114	117	122
6	91	94	99	104	110	115	118	123
7	92	95	100	106	111	116	119	125
8	94	97	102	107	113	118	121	126
9	95	98	103	109	114	119	122	128
10	97	100	105	110	116	121	124	129
11	98	101	106	112	117	122	125	131
12	100	103	107	113	118	123	126	132
13	101	104	109	114	120	125	128	133
14	102	104	109	115	120	125	128	134
15	102	105	110	115	121	126	129	134
16	102	105	110	115	121	126	129	134
17	102	105	110	115	121	126	129	134
DIASTOLIC PRESSURE								
5	46	48	53	59	64	68	71	76
6	47	49	54	59	64	68	71	76
7	47	50	54	60	65	69	72	77
8	48	50	55	60	65	70	73	78
9	49	51	55	61	66	70	73	78
10	49	51	56	61	66	71	74	79
11	49	52	56	62	67	71	74	79
12	50	52	57	62	67	71	74	79
13	50	53	57	62	67	71	74	79
14	50	53	58	62	67	72	74	79
15	50	54	58	62	67	72	74	79
16	50	54	58	62	67	72	74	80
17	50	54	58	62	67	72	75	80

*The 99th percentile values were added after submission of the manuscript.

From Park MK, Menard SW, Schoolfield J: Oscillometric blood pressure standards for children, *Pediatr Cardiol* 2005 (in press).

TABLE B-7

DINAMAP (MODEL 1846) BP PERCENTILES FOR NEONATES TO 5-YEAR-OLD CHILDREN

AGE	Percentiles						
	5TH	10TH	25TH	MEAN	75TH	90TH	95TH
SYSTOLIC PRESSURE							
1-3 days	52	56	58	65	71	74	77
2-3 wks	62	66	71	78	84	89	92
1-5 mo	76	79	88	94	102	106	111
6-11 mo	79	84	88	94	99	104	109
1 yr	80	84	89	94	99	104	108
2 yr	82	85	91	95	101	106	109
3 yr	84	87	92	98	103	108	112
4 yr	86	90	95	100	105	110	114
5 yr	89	93	96	102	107	113	116
DIASTOLIC PRESSURE							
1-3 days	31	33	37	41	45	50	52
2-3 wks	31	37	42	47	63	58	61
1-5 mo	45	48	53	59	64	71	75
6-11 mo	41	44	52	57	63	67	69
1 yr	44	48	52	57	73	67	69
2 yr	45	47	52	56	61	65	68
3 yr	44	47	52	56	61	65	69
4 yr	44	48	52	56	61	65	68
5 yr	44	48	53	57	62	66	68

Data presented in graphic form in Park M, Menard SM: Normative oscillometric BP values in the first 5 years in an office setting, Arch J Dis Child 143:860-864, 1989.

TABLE B-8
AMBULATORY BLOOD PRESSURE STANDARDS FOR DAYTIME AND NIGHTTIME,
ACCORDING TO HEIGHT: BOYS

HEIGHT (CM)	Systolic BP				Diastolic BP			
	Daytime		Nighttime		Daytime		Nighttime	
	90TH PCT	95TH PCT	90TH PCT	95TH PCT	90TH PCT	95TH PCT	90TH PCT	95TH PCT
120	120.6	123.5	103.7	106.4	79.1	81.2	61.9	64.1
125	121.0	124.0	104.9	107.8	79.3	81.3	62.2	64.3
130	121.6	124.6	106.3	109.5	79.3	81.4	62.4	64.5
135	122.2	125.2	107.7	111.3	79.3	81.3	62.7	64.8
140	123.0	126.0	109.3	113.1	79.2	81.2	62.9	65.0
145	124.0	127.0	110.7	114.7	79.1	81.1	63.1	65.2
150	125.4	128.5	111.0	115.9	79.1	81.0	63.3	65.4
155	127.2	130.2	113.1	117.0	79.2	81.1	63.4	65.6
160	129.2	132.3	114.3	118.0	79.3	81.3	63.6	65.7
165	131.3	134.5	115.5	119.1	79.7	81.7	63.7	65.8
170	133.5	136.7	116.8	120.2	80.1	82.2	63.8	65.9
175	135.6	138.8	118.1	121.2	80.6	82.8	63.8	65.9
180	137.7	140.9	119.2	122.1	81.1	83.4	63.8	65.8
185	139.8	143.0	120.3	123.0	81.7	84.1	63.8	65.8

PCT, percentile.
From Wühl E, Witte K, Soergel M, et al: Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions, *J Hypertens* 20:1995-2007, 2002.

TABLE B-9

**AMBULATORY BLOOD PRESSURE STANDARDS FOR DAYTIME AND NIGHTTIME,
ACCORDING TO HEIGHT: GIRLS**

HEIGHT (CM)	Systolic BP				Diastolic BP			
	Daytime		Nighttime		Daytime		Nighttime	
	90TH PCT	95TH PCT	90TH PCT	95TH PCT	90TH PCT	95TH PCT	90TH PCT	95TH PCT
120	118.5	121.1	105.7	109.0	79.7	81.8	64.0	66.4
125	119.5	122.1	106.4	109.8	79.7	81.8	63.8	66.2
130	120.4	123.1	107.2	110.6	79.7	81.8	63.6	66.0
135	121.4	124.1	107.9	113.9	79.7	81.8	63.4	65.8
140	122.3	125.1	108.4	111.9	79.8	81.8	63.2	65.7
145	123.4	126.3	109.1	112.5	79.8	81.8	63.0	65.6
150	124.6	127.5	109.9	113.1	79.9	81.9	63.0	65.5
155	125.7	128.5	110.6	113.8	79.9	81.9	62.9	65.5
160	126.6	129.3	111.1	114.0	79.9	81.9	62.8	65.4
165	127.2	129.8	111.2	114.0	79.9	81.9	62.7	65.2
170	127.5	130.0	111.2	114.0	79.9	81.8	62.5	65.0
175	127.6	129.9	111.2	114.0	79.8	81.7	62.3	64.7

From Wühl E, Witte K, Soergel M, et al: Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions, *J Hypertens* 20:1995-2007, 2002.

TABLE C-1

ESTIMATED VALUE FOR PERCENTILE REGRESSION OF WAIST CIRCUMFERENCE FOR EUROPEAN-AMERICAN CHILDREN AND ADOLESCENTS ACCORDING TO SEX*

AGE (YR)	Percentile for Boys					Percentile for Girls				
	10TH	25TH	50TH	75TH	90TH	10TH	25TH	50TH	75TH	90TH
2	42.9	46.9	47.1	48.6	50.6	43.1	45.1	47.4	49.6	52.5
3	44.7	48.8	49.2	51.2	54.0	44.7	46.8	49.3	51.9	55.4
4	46.5	50.6	51.3	53.8	57.4	46.3	48.5	51.2	54.2	58.2
5	48.3	52.5	53.3	56.5	60.8	47.9	50.2	53.1	56.5	61.1
6	50.1	54.3	55.4	59.1	64.2	49.5	51.8	55.0	58.8	64.0
7	46.5	50.6	51.3	53.8	57.4	46.3	48.5	51.2	54.2	58.2
8	48.3	52.5	53.3	56.5	60.8	47.9	50.2	53.1	56.5	61.1
9	50.1	54.3	55.4	59.1	64.2	49.5	51.8	55.0	58.8	64.0
10	46.5	50.6	51.3	53.8	57.4	46.3	48.5	51.2	54.2	58.2
11	59.1	63.6	65.8	72.2	81.1	57.5	60.2	64.4	70.3	78.3
12	60.9	65.5	67.9	74.9	84.5	59.1	61.9	66.3	72.6	81.2
13	62.7	67.4	70.0	77.5	87.9	60.7	63.6	68.2	74.9	84.1
14	64.5	69.2	72.1	80.1	91.3	62.3	65.3	70.1	77.2	86.9
15	66.3	71.1	74.1	82.8	94.7	63.9	67.0	72.0	79.5	89.8
16	68.1	72.9	76.2	85.4	98.1	65.5	68.6	73.9	81.8	92.7
17	69.9	74.8	78.3	88.0	101.5	67.1	70.3	75.8	84.1	95.5
18	71.7	76.7	80.4	90.6	104.9	68.7	72.0	77.7	86.4	98.4

*Waist circumference was measured with a tape at just above the uppermost lateral border of the right ileum at the end of normal expiration.

From Fernandez JR, Redden DT, Pietrobelli A, Allison DB: Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents, J Pediatr 145:439-444, 2004.

TABLE C-2

ESTIMATED VALUE FOR PERCENTILE REGRESSION OF WAIST CIRCUMFERENCE FOR AFRICAN-AMERICAN CHILDREN AND ADOLESCENTS ACCORDING TO SEX*

AGE (YR)	Percentile for Boys					Percentile for Girls				
	10TH	25TH	50TH	75TH	90TH	10TH	25TH	50TH	75TH	90TH
2	43.2	44.6	46.4	48.5	50.0	43.0	44.6	46.0	47.7	50.1
3	44.8	46.3	48.3	50.7	53.2	44.6	46.3	48.1	50.6	53.8
4	46.3	48.0	50.1	52.9	56.4	46.1	48.0	50.2	53.4	57.5
5	47.9	49.7	52.0	55.1	59.6	47.7	49.7	52.3	56.2	61.1
6	49.4	51.4	53.9	57.3	62.8	49.2	51.4	54.5	59.0	64.8
7	51.0	53.1	55.7	59.5	66.1	50.8	53.2	56.6	61.8	68.5
8	52.5	54.8	57.6	61.7	69.3	52.4	54.9	58.7	64.7	72.2
9	54.1	56.4	59.4	63.9	72.5	53.9	56.6	60.9	67.5	75.8
10	55.6	58.1	61.3	66.1	75.7	55.5	58.3	63.0	70.3	79.5
11	57.2	59.8	63.2	68.3	78.9	57.0	60.0	65.1	73.1	83.2
12	58.7	61.5	65.0	70.5	82.1	58.6	61.7	67.3	75.9	86.9
13	60.3	63.2	66.9	72.7	85.3	60.2	63.4	69.4	78.8	90.5
14	61.8	64.9	68.7	74.9	88.5	61.7	65.1	71.5	81.6	94.2
15	63.4	66.6	70.6	77.1	91.7	63.3	66.8	73.6	84.4	97.9
16	64.9	68.3	72.5	79.3	94.9	64.8	68.5	75.8	87.2	101.6
17	66.5	70.0	74.3	81.5	98.2	66.4	70.3	77.9	90.0	105.2
18	68.0	71.7	76.2	83.7	101.4	68.0	72.0	80.0	92.9	108.9

*Waist circumference was measured with a tape at just above the uppermost lateral border of the right ileum at the end of normal expiration.

From Fernandez JR, Redden DT, Pietrobelli A, Allison DB: Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents, J Pediatr 145:439-444, 2004.

TABLE C-3

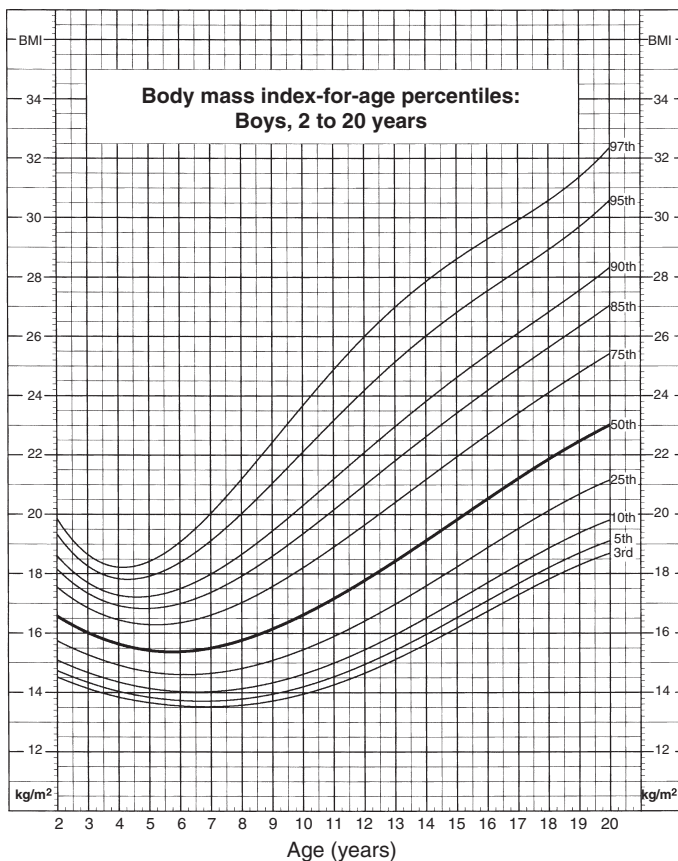
ESTIMATED VALUE FOR PERCENTILE REGRESSION OF WAIST CIRCUMFERENCE FOR MEXICAN-AMERICAN CHILDREN AND ADOLESCENTS ACCORDING TO SEX*

AGE (YR)	Percentile for Boys					Percentile for Girls				
	10TH	25TH	50TH	75TH	90TH	10TH	25TH	50TH	75TH	90TH
2	44.4	45.6	47.6	49.8	53.2	44.5	45.7	48.0	50.0	53.5
3	46.1	47.5	49.8	52.5	56.7	46.0	47.4	50.1	52.6	56.7
4	47.8	49.4	52.0	55.3	60.2	47.5	49.2	52.2	55.2	59.9
5	49.5	51.3	54.2	58.0	63.6	49.0	51.0	54.2	57.8	63.0
6	51.2	53.2	56.3	60.7	67.1	50.5	52.7	56.3	60.4	66.2
7	52.9	55.1	58.5	63.4	70.6	52.0	54.5	58.4	63.0	69.4
8	54.6	57.0	60.7	66.2	74.1	53.5	56.3	60.4	65.6	72.6
9	56.3	58.9	62.9	68.9	77.6	55.0	58.0	62.5	68.2	75.8
10	58.0	60.8	65.1	71.6	81.0	56.5	59.8	64.6	70.8	78.9
11	59.7	62.7	67.2	74.4	84.5	58.1	61.6	66.6	73.4	82.1
12	61.4	64.6	69.4	77.1	88.0	59.6	63.4	68.7	76.0	85.3
13	63.1	66.5	71.6	79.8	91.5	61.1	65.1	70.8	78.6	88.5
14	64.8	68.4	73.8	82.6	95.0	62.6	66.9	72.9	81.2	91.7
15	66.5	70.3	76.0	85.3	98.4	64.1	68.7	74.9	83.8	94.8
16	68.2	72.2	78.1	88.0	101.9	65.6	70.4	77.0	86.4	98.0
17	69.9	74.1	80.3	90.7	105.4	67.1	72.2	79.1	89.0	101.2
18	71.6	76.0	82.5	93.5	108.9	68.6	74.0	81.1	91.6	104.4

*Waist circumference was measured with a tape at just above the uppermost lateral border of the right ileum at the end of normal expiration.

From Fernandez JR, Redden DT, Pietrobelli A, Allison DB: Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents, J Pediatr 145:439-444, 2004.

CDC Growth Charts: United States

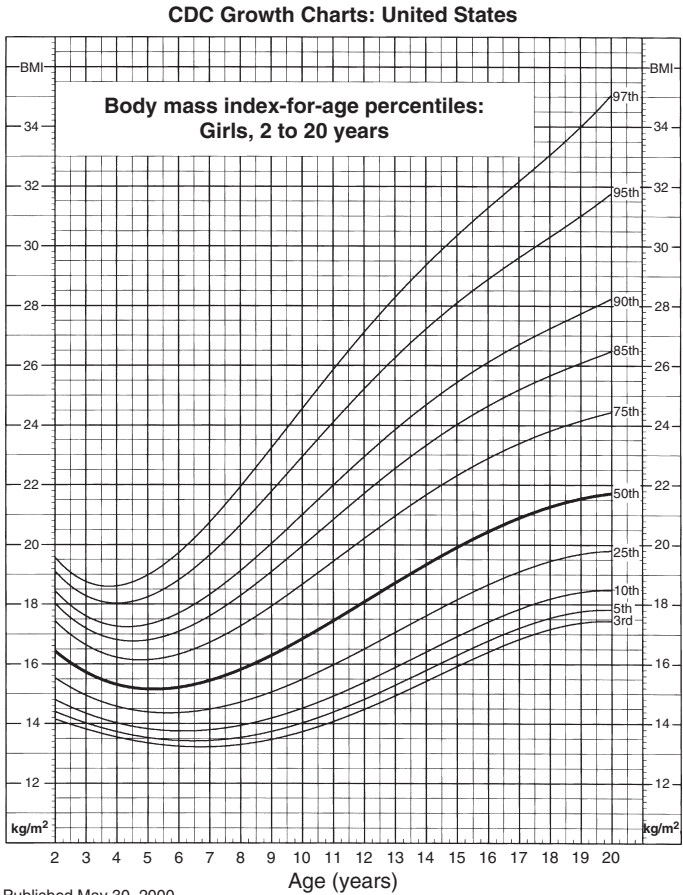


Published May 30, 2000.

Source: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).

FIGURE C-1

Body mass index percentile curves for boys 2 to 20 years old.



Published May 30, 2000.

Source: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).

FIGURE C-2

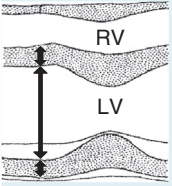
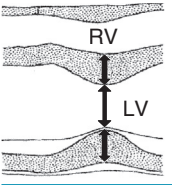
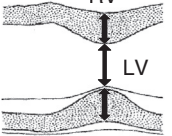
Body mass index percentile curves for girls 2 to 20 years old.

Appendix D

Normal Echocardiographic Values

TABLE D-1

TWO-DIMENSIONAL ECHOCARDIOGRAPHY-DERIVED M-MODE MEASUREMENTS OF THE LV DIMENSION AND WALL THICKNESS: MEAN (-2 SD TO $+2$ SD) (IN MM)*

VIEWS	BSA	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.2	1.4	1.6	1.8	2.0	2.2
	RV	19.5	23.0	26.0	29.5	31.5	33.5	35.5	37.5	39.5	42.0	45.0	47.0	49.5	51.5	53.5
	EDD	(15.5-23.0)	(19.0-27.0)	(22.0-30.5)	(24.5-34.0)	(27.0-36.5)	(29.0-38.5)	(30.5-41.0)	(32.0-43.0)	(33.5-45.0)	(36.0-48.0)	(38.5-51.0)	(40.5-54.0)	(42.5-57.0)	(44.0-60.0)	(45.5-62.0)
	IVS (D)	4.5	5.0	5.0	5.5	6.0	6.0	6.5	7.0	7.0	8.0	8.5	9.0	9.5	10.5	11.0
	LVPW (D)	4.0	4.5	4.5	5.0	5.5	6.0	6.0	6.5	7.0	7.5	8.0	8.5	9.0	9.5	10.0
	RV	12.0	15.0	17.0	18.5	20.0	21.5	23.0	24.0	25.5	28.0	29.5	31.5	33.0	34.5	36.0
	ESD	(8.0-15.0)	(11.5-18.0)	(13.5-20.0)	(15.0-22.5)	(16.5-24.5)	(17.5-26.0)	(18.5-28.0)	(19.5-29.0)	(20.5-31.0)	(22.0-33.5)	(23.5-35.5)	(24.5-37.5)	(25.5-39.5)	(26.5-41.5)	(27.5-43.0)
	IVS (S)	6.5	7.0	7.5	8.0	8.5	9.0	9.5	9.5	10.0	10.5	11.5	12.0	12.5	13.5	14.0
	LVPW (S)	6.5	7.0	8.0	9.0	9.5	10.0	10.5	11.5	11.5	12.5	13.0	14.0	14.5	15.0	16.0
	(S)	(5.5-8.0)	(6.0-8.5)	(6.5-9.5)	(7.0-10.5)	(7.5-11.0)	(8.0-12.0)	(8.5-12.5)	(9.0-13.5)	(9.0-14.0)	(10.0-15.0)	(10.5-16.0)	(11.0-17.5)	(11.0-18.5)	(11.5-19.5)	(12.0-20.0)

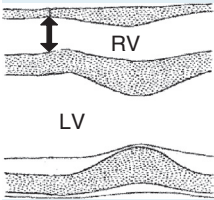
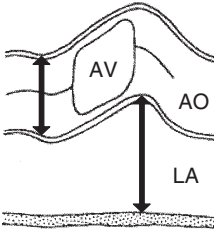
*Values are rounded off to the nearest 0.5 mm.

BSA, body surface area; IVS (D), interventricular septal thickness, end diastolic; IVS (S), interventricular septal thickness, end systolic; LVEDD, LV end diastolic dimension; LVESD, LV end systolic dimension; LVPW (D), LV posterior wall thickness, end diastolic; LVPW (S), LV posterior wall thickness, end systolic; SD, standard deviation.

Values have been derived from graphic data of Lai WW, Mertens LL, Cohen MS, Geva T (eds): Appendix 1. In Echocardiography in Pediatric and Congenital Heart Disease, Wiley-Blackwell, Oxford (UK), 2010.

TABLE D-2

STAND-ALONE M-MODE ECHOCARDIOGRAPHIC MEASUREMENTS: RIGHT VENTRICLE, AORTA, LEFT ATRIUM BY BODY SURFACE AREA: MEAN (90% TOLERANCE LIMITS) (IN MM)*

ECHO VIEWS	BSA	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.2	1.4	1.6	1.8	2.0
	RV (diastolic)	7 (-16)	9.5 (0-17)	10 (0-17)	10 (2.5-18)	11 (3-19)	12 (3.5-21)	13 (4-22)	14 (4.5-23)	14 (5-24)	16 (6-26)	18 (6.5-29)	20 (7-32)	22 (7.5-35)	23 (8-42)
	Aorta (diastolic)	10 (6-14)	12 (7.5-16)	13 (9-17.5)	14 (9.5-19)	15 (10.5-21)	16 (11.5-22)	17 (12.5-24)	18 (13-24.5)	19 (13.5-25)	21 (14.5-27)	22 (15.5-29)	23 (16-30.5)	24 (16-32)	24 (16-33)
	LA (systolic)	13 (6-20)	16 (8-23)	18 (9-25)	19 (11-27)	20 (12-29)	22 (13-31)	23 (14-33)	24 (15-34)	26 (16-35)	27 (17-38)	28 (17-40)	29 (18-42)	29 (18-43)	30 (18-44)


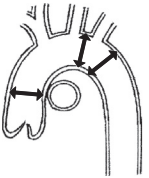
*Values rounded off to the nearest 0.5 mm or measurements <10 mm and to the nearest 1 mm for measurements ≥10 mm.

BSA, body surface area; LA, left atrium; RV, right ventricle.

Values have been derived from graphic data of Roge CL, Silverman NH, Hart PA, Ray RM: Cardiac structure growth pattern determined by echocardiography, Circulation 57:285-290, 1978.

TABLE D-3

TWO-DIMENSIONAL ECHOCARDIOGRAPHIC MEASUREMENTS OF AORTIC ROOT AND AORTA: MEAN (–2 SD TO +2 SD) (IN MM)*

ECHO VIEWS	BSA	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.2	1.4	1.6	1.8	2.0	2.2
	Aortic annulus	7.0 (5.5-9.0)	8.5 (7.0-10.0)	10.0 (8.0-12.0)	11.0 (9.0-13.5)	12.0 (10.0-14.5)	13.5 (11.0-15.5)	14.0 (11.5-16.5)	15.0 (12.5-17.5)	15.5 (13.9-18.5)	17.5 (14.5-20.5)	18.5 (15.0-22.0)	20.0 (16.0-23.5)	21.0 (17.0-25.0)	22.0 (18.0-26.0)	23.0 (18.5-27.5)
	Sinus of Valsalva	9.5 (7.0-12.0)	11.5 (9.0-14.0)	13.0 (10.0-16.0)	14.5 (11.5-17.5)	16.0 (13.0-19.5)	17.5 (14.0-21.0)	18.5 (15.5-22.05)	19.5 (15.5-23.5)	20.5 (16-25.0)	22.0 (18.0-27.0)	24.0 (19.0-30.0)	25.5 (20.0-31.5)	27.0 (21.0-33.5)	28.5 (22.0-35.5)	30.5 (23.0-38.5)
	Sinotubular junction	8.0 (6.0-10.0)	10.0 (7.5-12.0)	11.0 (9.0-13.5)	12.5 (10.0-15.0)	14.0 (11.0-16.5)	15.0 (12.0-18.0)	16.0 (12.5-19.0)	16.5 (13.0-20.5)	17.5 (14.0-21.5)	19.5 (15.5-24.0)	21.0 (16.5-26.0)	22.0 (17.0-27.5)	24.0 (18.0-29.0)	25.0 (19.0-31.0)	26.0 (20.0-32.0)
	Ascending-aorta	8.0 (5.5-11.0)	10.0 (7.0-13.0)	11.5 (8.5-15.0)	13.0 (10.0-16.0)	14.5 (11.0-17.5)	15.5 (12.0-19.0)	16.5 (13.0-20.5)	17.5 (14.0-21.5)	18.5 (14.5-23.0)	20.5 (15.5-25.5)	22.0 (16.5-27.5)	24.0 (18.0-29.5)	25.5 (19.0-31.0)	26.5 (20.0-33.0)	28.0 (21.0-35.0)
	Transverse aorta	6.5 (4.0-8.5)	8.0 (5.5-10.0)	9.5 (8.0-13.0)	10.5 (8.0-13.0)	11.5 (9.0-14.5)	12.5 (9.5-15.5)	13.0 (10.0-17.0)	14.0 (11.0-18.0)	15.0 (11.5-19.0)	17.0 (12.5-20.5)	18.0 (14.0-22.0)	19.5 (15.0-24.0)	20.5 (15.5-25.5)	21.5 (16.0-27.0)	22.5 (17.0-28.5)
	Aortic isthmus	5.5 (3.0-7.5)	6.5 (4.0-9.0)	7.5 (5.0-10.0)	8.5 (6.0-11.0)	9.5 (6.5-12.5)	10.5 (7.0-13.5)	11.0 (7.5-14.5)	12.0 (8.0-15.5)	12.5 (8.5-16.0)	13.5 (9.5-17.5)	15.0 (10.0-19.5)	16.0 (10.5-21.0)	17.0 (11.0-22.0)	17.5 (11.5-23.5)	18.0 (12.0-25.0)

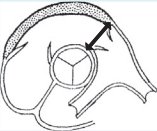
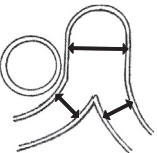
*Values are rounded off to the nearest 0.5 mm.

BSA, body surface area; SD, standard deviation.

Values have been derived from graphic data of Lai WW, Mertens LL, Cohen MS, Geva T (eds): Appendix 1. In Echocardiography in Pediatric and Congenital Heart Disease, Wiley-Blackwell, Oxford (UK), 2010.

TABLE D-4

TWO-DIMENSIONAL ECHOCARDIOGRAPHIC MEASUREMENTS OF THE PULMONARY VALVE AND PULMONARY ARTERIES: MEAN (−2 SD TO +2 SD) (IN MM)*

ECHO VIEWS	BSA	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.2	1.4	1.6	1.8	2.0	2.2
	Pulmonary annulus	8.5 (6.0-10.5)	10.0 (8.0-12.5)	11.5 (9.0-14.0)	13.0 (10.0-16.0)	14.0 (11.0-17.5)	15.5 (11.5-19.0)	16.5 (12.0-20.5)	17.5 (13.0-21.5)	18.5 (13.5-23.0)	20.0 (15.0-25.0)	22.0 (16.0-27.5)	23.5 (17.0-29.0)	25.0 (18.0-30.5)	26.0 (19.0-33.0)	27.0 (19.5-34.0)
	Main PA	7.5 (5.0-10.0)	9.0 (6.5-12.0)	10.5 (7.5-14.0)	12.0 (9.0-15.0)	13.0 (9.5-16.5)	14.0 (10.0-17.5)	15.0 (11.0-18.5)	16.0 (11.5-20.0)	17.0 (12.0-21.0)	18.5 (13.5-23.0)	20.0 (14.5-25.5)	21.0 (15.0-28.0)	22.5 (16.0-30.0)	24.0 (16.5-32.0)	25.0 (17.0-33.0)
	Right PA	5.0 (3.5-7.0)	6.0 (4.5-8.0)	7.0 (5.0-9.0)	8.0 (5.5-10.0)	9.0 (6.0-11.0)	9.5 (6.5-12.0)	10.0 (7.0-13.0)	10.5 (7.5-13.5)	11.0 (8.0-14.0)	12.5 (9.0-16.0)	13.0 (9.5-17.5)	14.0 (10.0-18.5)	15.0 (10.5-20.0)	15.5 (10.5-21.0)	16.5 (11.0-22.0)
	Left PA	4.5 (3.0-6.5)	5.5 (4.0-7.5)	6.5 (4.5-8.5)	7.5 (5.0-9.5)	8.0 (5.5-10.5)	9.0 (6.0-11.0)	9.5 (6.5-12.0)	10.0 (7.0-13.0)	10.5 (7.5-14.0)	11.5 (8.0-15.5)	12.5 (8.5-16.5)	13.5 (9.0-18.0)	14.0 (9.0-19.0)	15.0 (9.5-20.0)	15.5 (10.0-21.0)

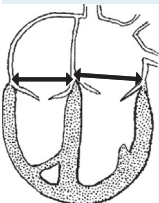
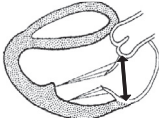
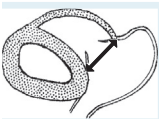
*Values are rounded off to the nearest 0.5 mm.

BSA, body surface area; SD, standard deviation.

Values have been derived from graphic data of Lai WW, Mertens LL, Cohen MS, Geva T (eds): Appendix 1. In Echocardiography in Pediatric and Congenital Heart Disease, Wiley-Blackwell, Oxford (UK), 2010.

TABLE D-5

TWO-DIMENSIONAL ECHOCARDIOGRAPHIC MEASUREMENTS OF ATRIOVENTRICULAR VALVES: MEAN (-2 SD TO $+2$ SD) (IN MM)*

ECHO VIEWS	BSA	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.2	1.4	1.6	1.8	2.0	2.2
	Mitral (Apical-4 chamber)	10.0 (8.0-12.0)	12.5 (9.5-15.0)	13.5 (10.5-17.5)	15.1 (12.0-19.0)	17.0 (12.5-21.0)	18.0 (13.5-22.5)	19.0 (14.5-24.0)	20.5 (15.0-25.5)	22.0 (15.5-27.5)	23.5 (16.5-30.5)	25.0 (17.5-33.0)	27.0 (18.0-35.5)	28.0 (18.5-37.5)	29.5 (19.0-40.0)	31.0 (19.0-42.0)
	Tricuspid (Apical-4 chamber)	11.0 (7.5-14.0)	13.0 (8.5-17.0)	15.0 (10.5-18.5)	17.0 (12.0-20.5)	18.0 (13.0-22.5)	19.0 (14.0-23.5)	20.0 (15.0-25.0)	21.5 (16.0-27.5)	22.5 (17.0-28.0)	24.0 (18.0-30.5)	26.5 (19.0-33.0)	28.0 (20.5-35.0)	29.5 (21.5-37.5)	31.0 (22.5-39.5)	32.5 (23.5-42.0)
	Mitral (Parasternal- long)	10.0 (7.5-12.5)	11.5 (9.0-15.0)	13.0 (10.0-16.0)	14.5 (11.0-18.0)	16.0 (12.0-19.5)	17.0 (12.5-21.0)	18.0 (13.0-22.5)	19.0 (14.0-23.0)	20.0 (15.0-25.0)	22.0 (16.0-27.5)	23.0 (17.0-30.0)	25.0 (18.0-32.0)	26.0 (18.5-34.5)	28.0 (19.0-37.0)	29.0 (20.0-39.0)
	Tricuspid (RV inflow view)	10.5 (7.5-13.0)	12.5 (9.0-15.5)	14.5 (10.5-17.5)	15.5 (12.5-19.5)	17.5 (13.0-22.0)	18.5 (14.0-23.0)	20.0 (15.0-25.0)	21.5 (16.0-27.0)	22.0 (17.0-28.0)	23.5 (17.5-30.5)	25.5 (18.5-33.0)	27.5 (19.5-35.5)	29.0 (20.5-38.0)	30.5 (21.5-40.0)	32.5 (22.5-42.5)

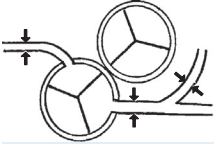
*Values are rounded off to the nearest 0.5 mm.

BSA, body surface area; SD, standard deviation.

Values have been derived from graphic data of Lai WW, Mertens LL, Cohen MS, Geva T (eds): Appendix 1. In Echocardiography in Pediatric and Congenital Heart Disease, Wiley-Blackwell, Oxford (UK), 2010.

TABLE D-6

TWO-DIMENSIONAL ECHOCARDIOGRAPHIC MEASUREMENTS OF MEAN AND PREDICTION LIMITS FOR 2 AND 3 STANDARD DEVIATIONS FOR MAJOR CORONARY ARTERY SEGMENTS*

ECHO VIEWS	BSA		0.2	0.3	0.4	0.5	0.6	0.7	0.8	1.0	1.2	1.4	1.6	1.8	2.0
	Left anterior descending (LAD)	Mean	1.2	1.4	1.6	1.8	1.9	2.0	2.2	2.3	2.5	2.7	2.8	2.9	3.0
		Mean +2 SD	1.5	1.8	2.1	2.3	2.5	2.7	2.8	3.0	3.3	3.5	3.7	4.0	4.2
		Mean +3 SD	1.7	2.0	2.3	2.5	2.8	3.0	3.2	3.4	3.8	4.0	4.3	4.5	4.7
	Right coronary artery (RCA)	Mean	1.3	1.4	1.6	1.7	1.8	2.0	2.1	2.3	2.5	2.7	2.8	3.0	3.2
		Mean +2 SD	1.9	2.1	2.3	2.4	2.6	2.7	2.8	3.1	3.4	3.6	3.8	4.0	4.3
		Mean +3 SD	2.2	2.4	2.6	2.8	3.0	3.1	3.3	3.5	3.8	4.1	4.3	4.5	4.8
	Left main coronary artery (LMCA)	Mean	1.7	1.9	2.1	2.3	2.4	2.5	2.7	2.9	3.1	3.3	3.4	3.6	3.7
		Mean +2 SD	2.3	2.6	2.8	3.0	3.3	3.4	3.6	3.9	4.2	4.4	4.6	4.8	5.1
		Mean +3 SD	2.7	3.0	3.2	3.4	3.7	3.9	4.0	4.3	4.7	4.9	5.2	5.5	5.8

*Measurements are made from inner edge to inner edge. Values are rounded off to the nearest 0.1 mm.

BSA, body surface area; SD, standard deviation.

Values are from graphic data of Kurotobi S, Nagai T, Kawakami N, Sano T: Coronary diameter in normal infants, children and patients with Kawasaki disease, *Pediatr Int.* 44:1-4, 2002.

Appendix E

Dosages of Drugs Used in Pediatric Cardiology

TABLE E-1

DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Acetylsalicylic acid (Aspirin)	<i>Children and adults:</i> Antiplatelet therapy: PO: 3-5 mg/kg, QD Antipyretic/analgesic: PO, PR: 10-15 mg/kg/dose, q4-6 hr (Max 4g/24 hr) Antiinflammatory: PO: 80-100 mg/kg/24 hr, TID-QID	Rash, nausea, hepatotoxicity, GI bleeding, bronchospasm, GI distress, tinnitus Contraindications: hepatic failure, bleeding disorder, hypersensitivity, children <16 yr old with chickenpox or flu symptoms (due to the associa- tion with Reye syndrome)	Tab: 325, 500 mg Tab, enteric-coated: 81, 165, 325, 500, 650 mg Tab, chewable: 81 mg Supp: 60, 80, 120, 125, 200, 300, 325, 600, 650 mg, and 1.2 g.
Adenosine (Adenocard) (Antiarrhythmic)	For SVT: <i>Children and adults:</i> IV: 100-200 mcg/kg Repeat q1-2 min, with increment of 50 mcg/kg, to maximum of 250 mcg/kg (Max single dose 12 mg)	Bronchospasm, chest pain, transient asystole, bradycardia and tachycardia Transient AV block in atrial flutter/ fibrillation (±)	Inj: 3 mg/mL (2, 4 mL)
Amiodarone (Cordarone) (Class III antiarrhythmic)	<i>Children:</i> IV (in emergency situation): Loading: 5 mg/kg, slow infusion over 30 min, followed by infusion of 7 mcg/kg/ min (which is calculated to deliver 10 mg/kg/24 hr). Switch to oral mainte- nance dose as soon as clinical condition permits PO: 10-20 mg/kg/24 hr (<i>infants</i>) or 10 mg/kg/24 hr (<i>children and adolescents</i>) in 2 doses for 5 to 14 days, followed by maintenance dose of 5-7 mg/kg once a day (<i>Therapeutic level:</i> 0.5-2.5 mg/L) <i>Adults:</i> PO: Loading: 800-1600 mg QD for 1-3 wk, then reduce to 600-800 mg QD for 1 mo Maintenance: 200-400 mg QD	Progressive dyspnea and cough (pulmonary fibrosis), worsening of arrhythmias, hepatotoxicity, nausea and vomiting, corneal micro- deposits, hypotension, heart block, ataxia, hypo- or hyperthyroidism, photosensitivity Contraindications: AV block, sinus node dysfunction, sinus bradycardia	Tab: 200, 400 mg Susp: 5 mg/mL Inj: 50 mg/mL

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Amlodipine (Norvasc) (Calcium channel blocker, antihypertensive)	For hypertension: <i>Children:</i> PO: Initial 0.1 mg/kg/dose QD-BID; may be increased gradually to a max of 0.6 mg/kg/24 hr <i>Adults:</i> PO: 5-10 mg/dose QD (Max 10 mg/24 hr)	Edema, dizziness, flushing, palpitation, headache, fatigue, nausea, abdominal pain, somnolence	Tab: 2.5, 5, 10 mg Susp: 1 mg/mL
	<i>Amrinone (Inocor)</i> (Noncatecholamine inotropic agent with vasodilator effects) <i>Children:</i> IV: <i>Loading:</i> 0.5 mg/Kg over 2-3 min in ½ NS (not D5W) <i>Maintenance:</i> 5-20 mcg/kg/min <i>Adults:</i> IV: <i>Loading:</i> 0.75 nmg/kg over 2-3 min <i>Maintenance:</i> 5-10 mcg/kg/min		
Atenolol (Tenormin) (β ₁ -adrenoceptor blocker, antihypertensive, antiarrhythmic)	<i>Children:</i> PO: 1-2 mg/kg/dose, QD <i>Adults:</i> PO: 25-100 mg/dose, QD for 1-2 wk (alone or with diuretic for hypertension); may increase to 200 mg QD	CNS symptoms (dizziness, tiredness, depression), bradycardia, postural hypotension, nausea and vomiting, rash, blood dyscrasias (agranulocytosis, purpura)	Tab: 25, 50, 100 mg Susp: 2 mg/mL Inj: 0.5 mg/mL (10 mL)
	<i>Children:</i> PO: Starting dose 10 mg QD for 4-6 wk; increase to 20 mg QD and 40 mg QD as needed (Adult max dose: 80 mg/24 hr)		
Atorvastatin (Lipitor) (Antilipemic, "statin," HMG-CoA reductase inhibitor)		Headache, constipation, diarrhea, elevated liver enzymes, rhabdomyolysis, myopathy	Tab: 10, 20, 40, 80 mg

Azathioprine (Imuran, Azasan) (Immunosuppressant)	<i>Children:</i> IV, PO: <i>Initial:</i> 3-5 mg/kg/24 hr, QD <i>Maintenance:</i> 1-3 mg/kg/24 hr (to produce WBC count around 5000/mm ³); may be reduced if WBC count falls below 4000/mm ³	Bone marrow suppression (leukopenia, thrombocytopenia, anemia), GI symptoms (nausea and vomiting)	Tab: 25, 50, 75, 100 mg Susp: 50 mg/mL Inj: 100 mg powder for reconst
Bosentan (Tracleer) (Nonselective endothelin receptor blocker)	For pulmonary hypertension: <i>Children:</i> PO: <20 kg: 31.25 mg BID 20-40 kg: 62.5 mg BID >40 kg: 125 mg BID <i>Adults:</i> PO: 125 mg BID	Liver dysfunction, decrease in hemoglobin, fluid retention, heart failure, headache	Tab: 62.5, 125 mg
Bumetanide (Bumex) (Loop diuretic)	<i>Children:</i> PO, IM, IV: >6 mo: 0.015-0.1 mg/kg/dose, QD-QOD <i>Adults:</i> PO: 0.5-2 mg/dose, QD-BID IV: 0.5-1 mg over 1-2 min, q2-3 hr PRN (Max 10 mg/24 hr)	Hypotension, cramps, dizziness, headache, electrolyte losses (hypokalemia, hypocalcemia, hyponatremia, hypochloremia), metabolic alkalosis	Tab: 0.5, 1, 2 mg Inj: 0.25 mg/mL
Calcium glubionate (Neo-Calglucon) 6.4% elemental calcium (Calcium supplement)	For neonatal hypocalcemia: PO: 1200 mg/kg/24 hr, q4-6 hr <i>Maintenance:</i> <i>Infants and children:</i> PO: 600-2000 mg/kg/24 hr, QID (Max 9 g/24 hr) <i>Adults:</i> PO: 6-18 g/24 hr, QID	GI irritation, diarrhea, dizziness, headache Best absorbed when given before meals.	Syrup: 1.8 g/5 mL (480 mL) (1.2 mEq Ca/mL)

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Captopril (Capoten) (ACE inhibitor, antihypertensive, vasodilator)	<i>Neonates:</i> PO: 0.1–0.4 mg/kg/24 hr, TID–QID	Neutropenia/agranulocytosis, proteinuria, hypotension and tachycardia, rash, taste impairment, hyperkalemia Evidence of fetal risk if given during 2nd and 3rd trimesters (same with all other ACE inhibitors)	Tab: 12.5, 25, 50, 100 mg Susp: 0.75, 1 mg/mL
	<i>Infants:</i> PO: Initially 0.15–0.3 mg/kg/dose, QD–QID; titrate upward if needed (Max 6 mg/kg/24 hr)		
	<i>Children:</i> PO: Initially 0.3–0.5 mg/kg/dose, TID; titrate upward if needed (Max 6 mg/kg/24 hr, BID–QID)		
	<i>Adolescents and Adults:</i> PO: Initially 12.5–25 mg/dose, BID–TID; increase weekly if needed by 25 mg/ dose to max dose of 450 mg/24 hr (Adjust dose with renal failure)		
	<i>Children:</i> PO: 50–100 mg/kg/24 hr, BID–TID; increase slowly as needed (Max 3 g/24 hr) <i>Adults:</i> PO: 330 mg–1 g/dose, BID–TID IV (<i>child and adult</i>): 50 mg/kg as loading dose, then 50 mg/kg/24 hr, q4–6 hr		
Carnitine (Carnitor)		Nausea and vomiting, abdominal cramp, diarrhea, seizure	Tab: 330, 500 mg Caps: 250 mg Oral sol: 100 mg/mL (118 mL) Inj: 200 mg/mL (5 mL)
Carvedilol (Coreg, Coreg CR) (Nonselective α - and β -adrenergic blocker)	<i>Children:</i> PO: Initial 0.09 mg/kg/dose, BID; increase gradually to 0.36 and 0.75 mg/kg as tolerated to adult max dose of 50 mg/24 hr <i>Adults:</i> PO: 3.125 mg, BID for 2 wk; increase slowly to a max dose of 25 mg BID as needed (for heart failure) (Max 25 mg BID for <85kg; 50 mg BID for >85 kg)	Dizziness, hypotension, headache, diarrhea, rarely AV block	Tab: 3.125, 6.125, 12.5, 25 mg Tab, extended release: 10, 20, 40, 80 mg

Chloral hydrate (Noctec, Aquachloral) (Sedative, hypnotic)	<p>As sedative: <i>Children:</i> PO, PR: 25-50 mg/kg/dose q6-8 hr Sedation for procedures: 25-100 mg (Max dose 2g) <i>Adults:</i> PO, PR: 250 mg/dose q8 hr</p> <p>As hypnotic: <i>Adults:</i> PO, PR: 500-2000 mg/dose</p>	Mucous membrane irritation (laryngospasm if aspirated), GI irritation, excitement/delirium, hypotension Contraindicated in hepatic and renal impairment	Caps: 500 mg Syrup: 250, 500 mg/5 mL Supp: 324, 500, 648 mg
Chlorothiazide (Diuril) (Diuretic)	<p><i>Children:</i> PO: 20-40 mg/kg/24 hr, BID IV: 2-8 mg/kg/24 hr, BID <i>Adults:</i> PO, IV: 250-2000 mg/dose QD-BID</p>	Hypercalcemia, hyperbilirubinemia, hyperglycemia, hyperuricemia, hypochloremic alkalosis, hypokalemia, hyponatremia, prerenal azotemia, hyperlipidemia, rarely pancreatitis, blood dyscrasias, allergic reactions	Tab: 250, 500 mg Susp: 250 mg/5 mL (237 mL) Inj: 500 mg powder for reconst with 18 mL sterile water
Cholestyramine (Questran, Prevalite) (Antilipemic, bile acid sequestrant)	<p><i>Children:</i> PO: 250-1500 mg/kg/24 hr, BID-QID <i>Adults:</i> PO: <i>Starting:</i> 1 packet (or scoopful) of Questran powder or Questran Light 1 to 2 times/day <i>Maintenance:</i> 2 to 4 packets or scoopfuls/24 hr in 2 doses (or 1 to 6 doses) (Max 6 packets/24 hr)</p>	Constipation and other GI symptoms, bleeding, hyperchloremic acidosis	Packet of 9-g Questran powder or 5-g Questran Light, each packet containing 4 g anhydrous cholestyramine resin
Clofibrate (Atromid-S) (Antilipemic, triglyceride-lowering agent)	<p><i>Children:</i> PO: 0.5-1.5 mg/24 hr, BID-TID <i>Adults:</i> PO: <i>Initial and maintenance:</i> 2 g/24 hr, BID-TID</p>	Nausea and other GI symptoms (vomiting, diarrhea, flatulence), headache, dizziness, fatigue, rash, blood dyscrasias, myalgia, arthralgia, hepatic dysfunction	Caps: 500 mg

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Clopidogrel (Plavix) (Antiplatelet)	<i>Children:</i> PO: 1 mg/kg/24 hr to max (adult dose) of 75 mg/24 hr <i>Adults:</i> PO: 75 mg/dose, QD	Bleeding, especially when used with aspirin, neutropenia or agranulocytosis, abdominal pain, constipation, rash, syncope, palpitation	Tab: 75 mg
Colestipol (Colestid) (Antilipemic, bile acid sequestrant)	<i>Children:</i> PO: 300–1500 mg/24 hr in 2–4 doses <i>Adults:</i> PO: <i>Starting dose:</i> 5 g 1–2 times/24 hr; increment of 5 g q1–2 mo <i>Maintenance:</i> 5–30 g/24 hr, BID–QID (mix with 3–6 oz water or another fluid)	Constipation and other GI symptoms (abdominal distention, flatulence, nausea and vomiting, diarrhea), rarely rash, muscle and joint pain, headache, dizziness	Packet: 5 g
Cyclosporine, Cyclosporine microemulsion (Sandimmune, Gengraf, Neoral) (Immunosuppressant)	<i>Children:</i> PO: 15 mg/kg as a single dose given 4–12 hr pretransplant; give same daily dose for 1–2 wk posttransplant, then reduce by 5% per wk to 5–10 mg/kg/24 hr, QD–BID (<i>Therapeutic level:</i> 100–300 ng/mL) IV: 5–6 mg/kg as a single dose given 4–12 hr pretransplant; administer over 2–6 hr; give same dose posttransplant until patient able to tolerate oral form For hypertensive crisis: <i>Children and adults:</i> IV: 1–3 mg/kg (max 150 mg single dose); repeat q5–15 min; titrate to desired effect	Nephrotoxicity, tremor, hypertension, less commonly hepatotoxicity, hyperlipidemia, hirsutism, gum hypertrophy, rarely lymphoma, hypomagnesemia	Oral sol: 100 mg/mL (50 mL) Neoral sol: 100 mg/mL (50 mL) Caps: 25, 50, 100 mg Neoral caps: 25, 100 mg Inj: 50 mg/mL
Diazoxide (Hyperstat IV, Proglycem) (Antihypertensive, peripheral vasodilator)		Hypotension, transient hyperglycemia, nausea and vomiting, sodium retention (CHF±)	Inj: 15 mg/mL

Digoxin (Lanoxin, Digitek) (Cardiac glycoside, antiarrhythmic, inotrope)	<p>Children: PO: Total digitalizing dose: Premature infant: 20 mcg/kg; Full-term newborn: 30 mcg/kg; Child 1 mo–2 yr: 40–50 mcg/kg; Child >2–10 yr: 30–40 mcg/kg; >10 yr and <100 kg: 10–15 mcg/kg PO: Maintenance: 25%–30% of TDD/24 hr BID IV: 75%–80% of PO dose Adults: PO: Loading: 8–12 mcg/kg Maintenance: 0.10–0.25 mg/24 hr (Therapeutic level: 0.8–2 ng/mL)</p>	AV conduction disturbances, arrhythmias, nausea and vomiting	Elixir: 50 mcg/mL (60 mL) Tab: 125, 250, mcg Caps: 50, 100, 200 mcg Inj: 100, 250 mcg/mL
Digoxin immune Fab (Digibind, Digifab) (Antidigoxin antibody)	<p>Infants and children: IV: 1 vial (40 mg) dissolved in 4 mL H₂O, over 30 min Adults: IV: 4 vials (240 mg)</p>	Allergic reaction (rare), hypokalemia, rapid AV conduction in atrial flutter	Inj: 38, 40 mg powder for reconst
Diltiazem (Cardizem, Cardizem SR, Cardizem CD, Dilacor XR, Tiazac) (Calcium channel blocker, antihypertensive)	<p>Children: PO: 1.5–2 mg/kg/24 hr, TID–QID (Max 3.5 mg/kg/24 hr) Adolescents: Immediate release: PO: 30–120 mg/dose, TID–QID; usual range 180–360 mg/24 hr Extended release: PO: 120–300 mg/24 hr QD–BID (BID dosing with Cardizem SR; QD dosing with Cardizem CD, Dilacor XR, and Tiazac)</p>	Dizziness, headache, edema, nausea and vomiting, heart block, arrhythmias Contraindicated in 2nd- and 3rd-degree AV block, sinus node dysfunction, acute MI with pulmonary congestion Maximum antihypertensive effect seen within 2 weeks	Tab: 30, 60, 90, 120 mg Tab, extended release: 120, 180, 240, 300, 360, 420 mg Caps, extended release: 60, 90, 120, 180, 240, 300, 360, 420 mg Inj: 5 mg/mL (5, 10 mL)

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Dipyridamole (Persantine) (Antiplatelet)	<i>Children:</i> PO: 2-6 mg/kg/24 hr, TID <i>Adults:</i> PO: 75-100 mg QID (As an adjunct to warfarin therapy. Not to use with aspirin)	Vasodilation, rarely dizziness, angina	Tab: 25, 50, 75 mg
Disopyramide (Norpace) (Class IA antiarrhythmic)	<i>Children:</i> PO: <1 yr: 10-30 mg/kg/24 hr, q6 hr; 1-4 yr: 10-20 mg/kg/24 hr, q6 hr; 4-12 yr: 10-15 mg/kg/24 hr, q6 hr; 12-18 yr: 6-15 mg/kg/24 hr, q6 hr (q4 hr dosing when using regular caps) <i>Adults:</i> PO: 150 mg/dose q6 hr or 300 mg (extended release) q12 hr (Max 1.6 g/24 hr) (Therapeutic level: 3-7 mg/L)	Heart failure or hypotension, anticholinergic effects (urinary retention, dry mouth, constipation), nausea and vomiting, hypoglycemia	Caps: 100, 150 mg Caps, CR: 100, 150 mg Susp: 1 mg/mL, 10 mg/mL
Dobutamine (Dobutrex) (β -adrenergic stimulator)	<i>Children:</i> IV infusion: 2.5-15 mcg/kg/min in D ₅ W or NS (incompatible with alkali solution) (Max 40 mcg/kg/min) <i>Adults:</i> IV infusion: 2.5-10 mcg/kg/min (Max 40 mcg/kg/min)	Tachyarrhythmias, hypertension, nausea and vomiting, headache Contraindicated in HOCM and atrial flutter/fibrillation	Inj: 12.5 mg/mL (20 mL)

Inj: 40, 80, 160 mg/mL (5, 10, 20 mL)

Tachyarrhythmias, nausea and vomiting, hypotension or hypertension, extravasation (tissue necrosis [treat with local infiltration of phentolamine])

Children:
IV: Effects are dose dependent:
2–5 mcg/kg/min—increases RBF and urine output (minimum effects on heart rate and cardiac output)
5–15 mcg/kg/min—increases heart rate, cardiac contractility, and cardiac output
>20 mcg/kg/min— α -adrenergic effects with decreased RBF (\pm)
(Incompatible with a alkali solution)

Dopamine (Intropin, Dopastat) (Natural catecholamine inotropic agent)

Enalapril, Enalaprilat (Vasotec)
(ACE inhibitor, vasodilator)

Children:

PO: 0.1 mg/kg/dose QD or BID
Increase PRN over 2 wks
(Max 0.5 mg/kg/24 hr)

Adults:

For CHF:

PO: Start with 2.5 mg, QD or BID
(Usual range 5–20 mg/24 hr)

For hypertension:

PO: Start with 5 mg, QD
(Usual dose 10–40 mg/24 hr)

Hypotension, dizziness, fatigue, headache, rash, diminishing taste, neutropenia, hyperkalemia, chronic cough

Evidence of fetal risk if given during 2nd and 3rd trimesters (same with all other ACE inhibitors)

Tab: 2.5, 5, 10, 20 mg (Enalapril)
Oral susp: 1 mg/mL
Inj: 1.25 mg/mL (Enalaprilat)

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Enoxaparin (Lovenox) (Low-molecular-weight heparin, anticoagulant)	For DVT treatment: <i>Infants <2 months:</i> SC: 1.5 mg/kg/dose, q12 hr <i>Infants ≥2 months to adults:</i> SC: 1 mg/kg/dose, q12 hr (Adjust dose to achieve target antifactor Xa levels of 0.5–1 units/mL) For DVT prophylaxis: <i>Infants <2 months:</i> SC: 1 mg/kg/dose, q12 hr <i>Infants ≥2 mo up to 18 yr:</i> SC: 0.5 mg/kg/dose, q12 hr <i>Adults:</i> SC: 30 mg, BID for 7–10 days	Bleeding Contraindicated in major bleeding and drug-induced thrombocytopenia Protamine sulfate is the antidote; 1 mg protamine sulfate neutralizes 1 mg enoxaparin	Inj: 100 mg/mL (3 mL)
Epinephrine (Adrenalin) (α -, β_1 -, and β_2 -adrenergic stimulator)	For asystole and bradycardia: <i>Children:</i> IV/ET: 0.1–0.3 mL/kg of 1:10,000 sol (or 0.01–0.03 mg/kg) q3–5 min For circulatory shock or heart failure: <i>Children:</i> IV: 0.1–1 mcg/kg/min; titrate to effect	Tachyarrhythmias, hypertension, nausea and vomiting, headache, tissue necrosis (\pm)	Inj: 0.1 mg/mL (1:10,000 sol, 10 mL prefilled syringe) 1 mg/mL (1:1000 sol, 1, 30 mL)

Esmolol (Brevibloc) (β_1 -selective adrenergic blocking agent, antihypertensive, class II antiar- rhythmic)	<p><i>Children:</i> <i>Loading:</i> IV: 100-500 mcg/kg over 1 min</p> <p><i>Maintenance:</i> IV: 25-100 mcg/kg/min; increase by 25-50 mcg/kg to a maximum of 300 mcg/kg/min (Usual maintenance dose 50-500 mcg/kg/min)</p>	Bronchospasm, CHF, hypotension, nausea and vomiting	Inj: 10, 20, 250 mg/mL
Ethacrynic acid (Edecrin) (Loop diuretic)	<p><i>Children:</i> PO: 1 mg/kg/dose, QD-TID (Max 3 mg/kg/24 hr) IV: 1 mg/kg/dose</p> <p><i>Adults:</i> PO: 50-100 mg, QD (Max 400 mg) IV: 0.5-1 mg/kg/dose or 50 mg/dose</p>	Dehydration, hypokalemia, prerenal azotemia, hyperuricemia, eighth cranial nerve damage (deafness), abnormal LFT, agranulocytosis or thrombocytopenia, GI irritation, rash	Tab: 25 mg Inj: 50 mg vial for reconst with 50 mL D ₅ W
Flecainide (Tambacor) (Class IC antiar- rhythmic)	<p>For sustained VT:</p> <p><i>Children:</i> PO: <i>Initial:</i> 1-3 mg/kg/24 hr, q8 hr (Usual range: 3-6 mg/kg/24 hr, q8 hr) Monitor serum level to adjust dose if needed</p> <p><i>Adults:</i> PO: 100 mg/dose BID; may increase by 50 mg q12 hr every 4 days to max dose of 600 mg/24 hr (Therapeutic level: 0.2-1 mg/L)</p>	Worsening of HF, bradycardia, AV block, dizziness, blurred vision, dyspnea, nausea, headache, increased PR and QRS duration	Tab: 50, 100, 150 mg Susp: 5, 20 mg/ml

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Fludrocortisone acetate (Florinef, Fluohydrisone) (Corticosteroid)	<i>For syncopal episodes:</i> <i>Children:</i> PO: 0.1 mg/dose, QD <i>Adults:</i> PO: 0.2 mg/dose, QD	Hypertension, hypokalemia, acne, rash, bruising, headache, GI ulcers, growth suppression Weight gain (1–2 kg in 2–3 wk)	Tab: 0.1 mg
Furosemide (Lasix, Furomide) (Loop diuretic)	<i>Children:</i> IV: 0.5–2 mg/kg/dose, BID–QID PO: 1–2 mg/kg/dose, QD–TID (Max 6 mg/kg/dose) <i>Adults:</i> IV, PO: 20–80 mg/24 hr, BID–QID	Hypokalemia, hyperuricemia, prerenal azotemia, ototoxicity, rarely bloody dyscrasias, rash	Oral liquid: 10 mg/mL, 40 mg/5 mL Tab: 20, 40, 80 mg Inj: 10 mg/mL
Heparin (Anticoagulant)	<i>Infants and children:</i> IV: <i>Initial:</i> 50 U/kg IV bolus <i>Maintenance:</i> 10–25 U/kg/hr or 50–100 U/kg q4 hr [Adjust dose to give APTT 1.5–2.5 times control, 6–8 hr after IV infusion (or 3.5–4 hr after intermittent injection)] <i>Adults:</i> IV: <i>Initial:</i> 10,000 U IV injection <i>Maintenance:</i> 5000–10,000 U q4–6 hr IV drip: <i>Initial dose:</i> 5000 U followed by 20,000–40,000 U/24 hr	Bleeding Antidote: protamine sulfate (1 mg per 100 U heparin in previous 4 hr)	Inj: 1000, 2000, 2500, 5000, 7500, 10,000, 20,000, 40,000 U/mL

Hydralazine (Apre-soline) (Peripheral vasodilator, antihypertensive)	<p>For hypertensive crisis:</p> <p><i>Children:</i> IM, IV: 0.15–0.2 mg/kg/dose; may be repeated q4–6 hr (Max 20 mg/dose)</p> <p><i>Adults:</i> IM, IV: 20–40 mg/dose; repeat q4–6 hr PRN</p> <p>For chronic hypertension:</p> <p><i>Children:</i> PO: 0.75–3 mg/kg/24 hr, BID–QID</p> <p><i>Adults:</i> PO: Start with 10 mg 4 times/24 hr for 3–4 days; increase to 25 mg/dose QID for 3–4 days; then up to 50 mg QID</p>	Hypotension, tachycardia and palpitation, lupus-like syndrome with prolonged use (fever, arthralgia, splenomegaly, and positive LE-cell preparation), blood dyscrasias	<p>Tab: 10, 25, 50, 100 mg</p> <p>Oral liquid: 1.25, 2, 4 mg/mL</p> <p>Inj: 20 mg/mL</p>
Hydrochlorothiazide (HydroDIURIL, Esidrix, Hydro-Par, Oretic) (Thiazide diuretic)	<p><i>Children:</i> PO: 2–4 mg/kg/24 hr, BID (Max 100 mg/24 hr)</p> <p><i>Adults:</i> PO: 25–100 mg/24 hr, QD–BID (Max 200 mg/24 hr)</p>	Same as for chlorothiazide	<p>Tab: 25, 50, 100 mg</p> <p>Caps: 12.5 mg</p> <p>Sol: 10 mg/mL (500 mL)</p>

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Ibuprofen (NeoProfen) (Nonsteroidal antiinflammatory)	For PDA closure in premature infants: <i>Neonates ≤32 weeks (500–1500 g):</i> IV: Initial dose 10 mg/kg, followed by two doses of 5 mg/kg after 24 and 48 hours (Hold 2nd and 3rd dose if urine output is <0.6 mL/kg/hr) <i>Children:</i> IV: <i>Loading:</i> 0.75 mg/kg over 2–3 min <i>Maintenance:</i> 5–10 mcg/kg/min <i>Adults:</i> IV: <i>Loading:</i> 0.75 mg/kg over 2–3 min <i>Maintenance:</i> 5–10 mcg/kg/min	Sepsis, anemia, interventricular hemorrhage, apnea, GI disorders, renal impairment Contraindicated in interventricular hemorrhage, thrombocytopenia, necrotizing enterocolitis, significant renal dysfunction	Inj: 17.1 mg/mL ibuprofen lysine equivalent to 10 mg/mL of ibuprofen (2 mL) Inj: 5 mg/mL (20 mL) Vial: 1 mg
Inamrinone (Inocor) (Phosphodies- terase type-III inhibitor) Indomethacin (Indocin) (Nonsteroidal antiinflammatory, antipyretic agent, PG synthesis inhibitor)	For PDA closure in premature infants: IV: <48 hr: 0.2, 0.1, and 0.1 mg/kg/dose, q12–24 hr 2–7 days: 0.2, 0.2, and 0.2 mg/kg/dose, q12–24 hr >7 days: 0.2, 0.25, and 0.25 mg/kg/dose, q12–24 hr <i>Children:</i> IV: 0.1–2 mcg/kg/min, titrated to desired effect <i>Adults:</i> IV: 2–20 mcg/min, titrated to desired effect (incompatible with alkali solution)	Thrombocytopenia, hypotension, tachyarrhythmias, hepatotoxicity, nausea and vomiting, fever GI or other bleeding, GI disturbances, renal impairment, electrolyte disturbances (↓ Na, ↑ K levels)	Inj: 0.2 mg/mL (1: 5000 sol: 1, 5 mL)

Ketamine (Ketalar) (General anesthetic)	For cyanotic spells: <i>Infants:</i> IM: 2–3 mg/kg Repeat smaller doses q30 min PRN IV: 1–3 mg/kg/dose over 60 sec Repeat smaller doses q30 min PRN <i>Children:</i> PO: <i>Initial:</i> 4 mg/kg/24 hr, BID (Max 40 mg/kg/24 hr) IV: (for hypertensive emergency) <i>Initial:</i> 0.2–1 mg/kg/dose q10 min PRN (Max 20 mg/dose)	Hypertension/tachycardia, respiratory depression or apnea, CNS symptoms (dreamlike state, confusion, agitation)	Inj: 10, 50, 100 mg/mL
Labetalol (Normodyne, Trandate) (α - and β -adrenergic antagonist)	<i>Children:</i> PO: <i>Initial:</i> 4 mg/kg/24 hr, BID (Max 40 mg/kg/24 hr) IV: (for hypertensive emergency) <i>Initial:</i> 0.2–1 mg/kg/dose q10 min PRN (Max 20 mg/dose)	Orthostatic hypotension, edema, CHF, bradycardia Contraindicated in asthma	Tab: 100, 200, 300 mg Susp: 10, 40 mg/mL Inj: 5 mg/mL (20, 40 mL)
Lidocaine (Xylocaine) (Class IB antiarrhythmic)	<i>Children:</i> IV: <i>Loading:</i> 1 mg/kg/dose slow IV, q5–10 min PRN <i>Maintenance:</i> 30 mcg/kg/min (Range 20–50 mcg/kg/min) <i>Adults:</i> IV: <i>Loading:</i> 1 mg/kg/dose q5 min <i>Maintenance:</i> 1–4 mg/min (Therapeutic level: 1.5–5 mg/L)	Seizure, respiratory depression, CNS symptoms (anxiety, euphoria, or drowsiness), arrhythmias, hypotension or shock	Inj: 0.5%, 1%, 1.5%, 2%, 4%, 10%, 20% (1% = 10 mg/mL)

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Lisinopril (Zestril, Prinvil) (ACE inhibitor, antihypertensive)	For hypertension: <i>Children</i> ≥6 yr: PO: <i>Initial:</i> 0.07 mg/kg/24 hr (max initial dose is 5 mg/24 hr), increase dose at 1–2 wk intervals (Max 0.6 mg/kg/day or 40 mg/24 hr) <i>Adults:</i> PO: <i>Initial:</i> 10 mg QD; may increase upward as needed to max dose of 80 mg/24 hr	Dry nonproductive cough, rash, hypotension, hyperkalemia, angioedema, rarely bone marrow depression Evidence of fetal risk if given during 2nd and 3rd trimesters (same with all other ACE inhibitors)	Tab: 2.5, 5, 10, 20, 30, 40 mg
Losartan (Cozaar) (Angiotensin II- receptor blocker)	For hypertension: <i>Children</i> ≥6 yr: PO: 0.7 mg/kg/24 hr, QD-BID (Max 50 mg/24 hr) <i>Adults:</i> PO: <i>Initial:</i> 50 mg, QD (Max 100 mg QD)	Hypotension, dizziness, nasal congestion, muscle cramps Evidence of fetal risk if given during 2nd and 3rd trimesters	Tab: 25, 50, 100 mg
Lovastatin (Mevacor) (Antilipemic, HMG-CoA reductase inhibitor)	Adolescents: PO: Starting dose 10 mg/24 hr QD for 6–8 wk; increase to 20 mg/24 hr for 8 wk, and then increase to 40 mg/24 hr for 8 wk <i>Adults:</i> PO: Starting dose 20 mg/day, QD-BID (range 40–80 mg/24 hr) (Max dose with concurrent amiodarone or verapamil use is 40 mg/24 hr)	Mild GI symptoms, myositis syndrome, elevated transaminase levels, increased CK levels	Tab: 10, 20, 40 mg

Methyldopa (Aldomet) (Antihypertensive)	<p>For hypertensive crisis:</p> <p><i>Children:</i></p> <p>IV: Start at 2–4 mg/kg/dose q6–8 hr (Max dose 65 mg/kg/24 hr or 3 g/24 hr, whichever is less)</p> <p><i>Adults:</i></p> <p>IV: 250–500 mg q6 hr (Max 1 g q6 hr)</p> <p>For hypertension:</p> <p><i>Children:</i></p> <p>PO: 10 mg/kg/24 hr, BID–QID</p> <p>May be increased or decreased</p> <p>(Max dose 65 mg/kg/24 hr or 3 g/24 hr, whichever is less)</p> <p><i>Adults:</i></p> <p>PO: 250 mg/dose, BID–TID for 2 days</p> <p>May be increased or decreased q2 days. (Usual dose: 0.5–2 g/24 hr, BID–QID)</p> <p>(Max 3 g/24 hr)</p>	Sedation, orthostatic hypotension and bradycardia, lupus-like syndrome, Coombs (+) hemolytic anemia and leukopenia, hepatitis or cirrhosis, colitis, impotence	Inj: 50 mg/mL (5 mL) Susp: 50 mg/mL Tab: 250, 500 mg
Metoprolol (Lopressor) (β -adrenoceptor blocker)	<p><i>Children >2 yr:</i></p> <p>PO: Initially 0.1–0.2 mg/kg/dose, BID; gradually increase to 1–3 mg/kg/24 hr</p> <p><i>Adults:</i></p> <p>PO: Initially 100 mg/24 hr, QD–TID</p> <p>May increase to 450 mg/24 hr, BID–TID</p> <p>(Usual dose 100–450 mg/24 hr)</p> <p>(Usually used with hydrochlorothiazide 25–100 mg/24 hr)</p>	CNS symptoms (dizziness, tiredness, depression), bronchospasm, bradycardia, diarrhea, nausea and vomiting, abdominal pain	Tab: 25, 50, 100 mg Tab, extended release: 25, 50, 100, 200 mg

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Metolazone (Zaroxolyn, Diulo, Mykrox) (Thiazide-like diuretic)	<i>Children:</i> PO: 0.2–0.4 mg/kg/24 hr, QD–BID <i>Adults:</i> PO: For hypertension: 2.5–5 mg QD For edema: 5–20 mg, QD	Electrolyte imbalance, GI disturbance, hyperglycemia, bone marrow depression, chills, hyperuricemia, hepatitis, rash May be more effective than thiazide diuretics in impaired renal function	Tab: 0.5 (Mykrox), 2.5, 5, 10 mg Susp: 1 mg/mL
Mexiletine (Mexitil) (Class IB antiar- hythmic)	<i>Children:</i> PO: 6–8 mg/kg/24 hr, BID–TID for 2–3 days; then 2–5 mg/kg/dose q6–8 hr Increase 1–2 mg/kg/dose q2–3 days until desired effect achieved (with food or antacid) <i>Adults:</i> PO: 200 mg q8 hr for 2–3 days Increase to 300–400 mg q8 hr (Usual dose 200–300 mg q8 hr) (Therapeutic level: 0.75–2 mcg/mL)	Nausea and vomiting, CNS symptoms (headache, dizziness, tremor, paresthesia, mood changes), rash, hepatic dysfunction (±)	Caps: 150, 200, 250 mg
Milrinone (Primacor) (Phosphodies- terase type-III inhibitor)	<i>Children:</i> IV: Loading: 10–50 mcg/kg over 10 min; then 0.1–1 mcg/kg/min <i>Adults:</i> IV: Loading: 50 mcg/kg over 10 min 0.5 mcg/kg/min (Range 0.375–0.75 mcg/kg/min)	Arrhythmias, hypotension, hypokale- mia, thrombocytopenia	Inj: 1 mg/mL (5, 10, 20 mL) Inj, premixed in D ₅ W: 200 mcg/mL (100, 200 mL)

Minoxidil (Loniten) (Peripheral vasodilator)	<p><i>Children <12 yr:</i> PO: 0.2 mg/kg/24 hr, QD-BID initially Increase 0.1–0.2 mg/kg/24 hr q3 days until desired effect achieved (Usual dose 0.25–1 mg/kg/24 hr, QD-BID; max 50 mg/24 hr)</p> <p><i>Children >12 yr and Adults:</i> PO: 5 mg/dose, QD initially May be increased to 10, 20, 40 mg, QD-BID q3-day interval (Usual dose 10–40 mg/24 hr, QD-BID; max 100 mg/24 hr)</p>	Reflex tachycardia and fluid retention (used with a β -blocker and diuretic), pericardial effusion, hypertrichosis, rarely blood dyscrasias (leukopenia, thrombocytopenia)	Tab: 2.5, 10 mg
Morphine sulfate (Narcotic, anal- gesic)	<p><i>Children:</i> SC, IM, IV: 0.1–0.2 mg/kg/dose q2–4 hr (Max 15 mg/dose)</p> <p><i>Adults:</i> SC, IM, IV: 2.5–20 mg/dose q2–6 hr PRN</p>	CNS depression, respiratory depression, nausea and vomiting, hypotension, bradycardia	Inj: 0.5, 1, 2, 4, 5, 8, 10, 15, 25, 50 mg/mL
Mycophenolate mofetil (CellCept) (Immunosuppres- sant)	<p><i>Children:</i> PO: 600 mg/m²/dose, BID (Maximum 2000 mg/24 hr) (Therapeutic level: 5–7 ng/mL)</p> <p><i>Adults:</i> PO/IV: 2000–3000 g/24 hr, BID</p>	Headache, GI symptoms, hyperten- sion, bone marrow suppression (anemia), fever, increased risk of developing lymphomas or other malignancies	Tab: 500 mg Caps: 250 mg Oral susp: 200 mg/ml Inj: 500 mg

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TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Nifedipine (Procardia, Adalat) (Calcium channel blocker)	For hypertrophic cardiomyopathy:		
	<i>Children:</i> PO: 0.5–0.9 mg/kg/24 hr, TID–QID	Hypotension, peripheral edema, CNS symptoms (headache, dizziness, weakness), nausea	Caps: 10, 20 mg Tab, sustained release (Adalat CC, Procardia XL): 30, 60, 90 mg
	For hypertension:		
	<i>Children:</i> PO: 0.25–0.5 mg/kg/24 hr, QD–BID (Max 3 mg/kg/24 hr up to 120 mg/24 hr) <i>Adults:</i> PO: Initially 10 mg/dose, TID Titrate up to 20 to 30 mg/dose, TID–QID over 7–14 days (Usual dose 10–20 mg TID; max dose 180 mg/24 hr)		
Nitroglycerine (Nitro-Bid, Tridil, Nitrostat) (Periph- eral vasodilator)	<i>Children:</i> IV: 0.5–1 mcg/kg/min Increase 1 mcg/kg/min q20 min to titrate to effect (Max 6 mcg/kg/min) (Dilute in D ₅ W or NS with final concentration <400 mcg/mL; light sensitive)		
	<i>Adults:</i> IV: Initial dose: 5 mcg/min through infusion pump Increase 5 mcg/min q3–5 min until desired effect achieved	Hypotension, tachycardia, headache, nausea and vomiting	Inj: 0.5, 5 mg/mL Inj, premixed in D ₅ W: 100, 200, 400 mcg/mL

Nitroprusside (Nipride) (Peripheral vasodilator)	<p><i>Children:</i> IV: 0.3–0.5 mcg/kg/min, titrate to effect with BP monitoring (Usual dose 3–4 mcg/kg/min; max dose 10 mcg/kg/min) (Dilute stock solution [50 mg] in 250–2000 mL D₅W; light sensitive)</p>	Hypotension, palpitation, and cyanide toxicity (metabolic acidosis earliest and most reliable evidence) Monitor thiocyanate level when used >48 hr and in patients with renal or hepatic dysfunction. Thiocyanate level should be <50 mg/L; cyanate levels >2 mcg/mL are toxic levels.	Inj: 25 mg/mL (2 mL) Inj: 50 mg for reconst with 2–3 mL D ₅ W
Norepinephrine (Levophed, levarterenol) (α_1 - and β_1 -adrenoceptor stimulant)	<p><i>Children:</i> IV: 0.1 mcg/kg/min IV infusion initially; increase dose to attain desired effect (Max 2 mcg/kg/min) <i>Adults:</i> IV: Start at 4 mcg/min IV infusion; titrate to effect. (Usual dose range 8–12 mcg/min)</p>	Hypertension, bradycardia (reflex), arrhythmias, tissue necrosis (treat with phenolamine infiltration)	Inj: 1 mg/mL (4 mL)
Phentolamine (Regitine) (α -adrenoceptor blocker)	<p>For diagnosis of pheochromocytoma: <i>Children:</i> IM, IV: 0.05–0.1 mg/kg/dose; repeat q5 min until hypertension is controlled; then q2–4 hr PRN <i>Adults:</i> IM, IV: 2.5–5 mg/dose; repeat q5 min until hypertension is controlled; then q2–4 hr PRN For treatment of extravasated α-adrenergic drugs: SC: Make a solution of 0.5–1 mcg/mL with NS. Inject 1–5 mL (in 5 divided doses) around the site of extravasation (Max 0.1–0.5 mg/kg or 5 mg total)</p>	Hypotension, tachycardia or arrhythmias, nausea and vomiting	Inj: 5 mg powder for reconst

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Phenylephrine (Neo-Synephrine) (α_1 -adrenoceptor stimulant)	For hypotension: <i>Children:</i> IM, SC: 0.1 mg/kg/dose q1–2 hr PRN (Max dose 5 mg) IV: 5–10 mcg/kg/dose IV bolus q10–15 min or 0.1–0.5 mcg/kg/min <i>Adults:</i> IM, SC: 2–5 mg/dose q1–2 hr PRN (Max dose 5 mg) IV: 0.1–0.5 mg/dose IV bolus q10–15 min PRN Start IV drip at 100–180 mcg/min (Usual maintain dose 40–60 mcg/min)	Arrhythmias, hypertension, angina	Inj: 10 mg/mL
Phenytoin (Dilantin) (Class IB antiarrhythmic, anticonvulsant)	<i>Children:</i> IV: 2–4 mg/kg/dose over 5–10 min followed by PO dose PO: 2–5 mg/kg/24 hr, BID–TID (<i>Therapeutic level:</i> 5–18 mcg/mL for arrhythmias, 10–20 mcg/mL for seizures) <i>Adults:</i> IV: 100 mg q5 min (total 500 mg) PO: 250 mg QID for 1 day, 250 mg/dose BID for 2 days, and 300–400 mg/24 hr, QD–QID	Rash, Stevens–Johnson syndrome, CNS symptoms (ataxia, dysarthria), lupus-like syndrome, blood dyscrasias, peripheral neuropathy, gingival hypertrophy	Susp: 125 mg/5 mL (240 mL) Tab, chewable: 50 mg (Infatab) Caps: 100 mg Caps, extended release: 30, 100, 200, 300 mg Inj: 50 mg/mL
Potassium chloride	Supplement in diuretic therapy: <i>Children:</i> PO: 1–2 mEq/kg/24 hr, TID–QID (or 0.8–1.5 mL 10% potassium chloride/kg/24 hr, or 0.4–0.7 mL 20% potassium chloride/kg/24 hr, TID–QID)	GI disturbances, ulcerations, hyperkalemia	Oral sol: 10% (1.3 mEq/mL), 20% (2.7 mEq/mL) Caps, sustained release: 8, 10 mEq Tabs, sustained release: 8, 10, 15, 20 mEq

Potassium gluconate	Supplement in diuretic therapy: <i>Children:</i> PO: 1-2 mEq/kg/24 hr TID-QID, or 0.8-1.5 mL/kg/24 hr TID-QID <i>Children (8-13 yr):</i> PO: Starting dose 10 mg QD for 4-6 wk Increase to 20 QD as needed. <i>Adolescents (14-18 yr):</i> PO: 40 mg QD (Adult max dose 40 mg/day) <i>Children:</i> PO: 5 mcg/kg as a test dose; then 25-150 mcg/kg/24 hr, QID <i>Adults:</i> PO: 1 mg/dose BID-TID initially Increase to 20 mg/24 hr, BID-QID (Usual dose 6-15 mg/24 hr) <i>Children:</i> IV: Loading: 2-6 mg/kg/dose over 5 min repeated q10-30 min (Max 100 mg) <i>Maintenance:</i> 20-80 mcg/kg/min (Max 2 g/24 hr) PO: 15-50 mg/kg/24 hr q3-6 hr (Max 4 g/24 hr) <i>Adults:</i> IV: Loading: 50-100 mg/dose q5 min PRN <i>Maintenance:</i> 1-6 mg/min PO: Immediate release 250-500 mg/dose q3-6 hr (sustained release 500-1000 mg/dose q6 hr) (Therapeutic level: 4-10 mcg/mL)	Same as for potassium chloride	Elixir: 1.3 mEq/mL
Pravastatin (Pravachol) (Antilipemic, HMG-CoA reductase inhibitor)	<i>Children (8-13 yr):</i> PO: Starting dose 10 mg QD for 4-6 wk Increase to 20 QD as needed. <i>Adolescents (14-18 yr):</i> PO: 40 mg QD (Adult max dose 40 mg/day) <i>Children:</i> PO: 5 mcg/kg as a test dose; then 25-150 mcg/kg/24 hr, QID <i>Adults:</i> PO: 1 mg/dose BID-TID initially Increase to 20 mg/24 hr, BID-QID (Usual dose 6-15 mg/24 hr) <i>Children:</i> IV: Loading: 2-6 mg/kg/dose over 5 min repeated q10-30 min (Max 100 mg) <i>Maintenance:</i> 20-80 mcg/kg/min (Max 2 g/24 hr) PO: 15-50 mg/kg/24 hr q3-6 hr (Max 4 g/24 hr) <i>Adults:</i> IV: Loading: 50-100 mg/dose q5 min PRN <i>Maintenance:</i> 1-6 mg/min PO: Immediate release 250-500 mg/dose q3-6 hr (sustained release 500-1000 mg/dose q6 hr) (Therapeutic level: 4-10 mcg/mL)	Headache, constipation, diarrhea, elevated liver enzymes, rhabdomyolysis, myopathy	Tabs: 10, 20, 40, 80 mg
Prazosin (Mini-press) (Postsynaptic α_1 -adrenergic blocker, antihypertensive)	<i>Children:</i> PO: 5 mcg/kg as a test dose; then 25-150 mcg/kg/24 hr, QID <i>Adults:</i> PO: 1 mg/dose BID-TID initially Increase to 20 mg/24 hr, BID-QID (Usual dose 6-15 mg/24 hr) <i>Children:</i> IV: Loading: 2-6 mg/kg/dose over 5 min repeated q10-30 min (Max 100 mg) <i>Maintenance:</i> 20-80 mcg/kg/min (Max 2 g/24 hr) PO: 15-50 mg/kg/24 hr q3-6 hr (Max 4 g/24 hr) <i>Adults:</i> IV: Loading: 50-100 mg/dose q5 min PRN <i>Maintenance:</i> 1-6 mg/min PO: Immediate release 250-500 mg/dose q3-6 hr (sustained release 500-1000 mg/dose q6 hr) (Therapeutic level: 4-10 mcg/mL)	CNS symptoms (dizziness, headache, drowsiness), palpitation, nausea	Caps: 1, 2, 5 mg
Procainamide (Procanbid, Pronestyl) (Class IA antiarrhythmic)	<i>Children:</i> IV: Loading: 2-6 mg/kg/dose over 5 min repeated q10-30 min (Max 100 mg) <i>Maintenance:</i> 20-80 mcg/kg/min (Max 2 g/24 hr) PO: 15-50 mg/kg/24 hr q3-6 hr (Max 4 g/24 hr) <i>Adults:</i> IV: Loading: 50-100 mg/dose q5 min PRN <i>Maintenance:</i> 1-6 mg/min PO: Immediate release 250-500 mg/dose q3-6 hr (sustained release 500-1000 mg/dose q6 hr) (Therapeutic level: 4-10 mcg/mL)	Nausea and vomiting, blood dyscrasias, rash, lupus-like syndrome, hypotension, confusion or disorientation	Tab, sustained release: 250, 500, 750, 1000 mg Caps: 250, 375, 500 mg Susp: 5, 50, 100 mg/mL Inj: 100, 500 mg/mL

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Propranolol (Inderal) (β -adrenoceptor blocker, class II antiarrhythmic)	For hypertension: <i>Children:</i> PO: 0.5–1 mg/kg/24 hr, BID–QID; may increase q3–5 days (Usual dose 2–4 mg/kg/24 hr; max dose 8 mg/kg/24 hr) For arrhythmias: <i>Children:</i> IV: 0.01–0.15 mg/kg/dose over 10 min; repeat q6–8 hr PRN (Max 1 mg/dose for infants; 3 mg/dose for children) PO: Start at 0.5–1 mg/kg/24 hr, TID–QID; increase dose q3–5 days PRN (Usual dose 2–4 mg/kg/24 hr; max dose 16 mg/kg/24 hr) <i>Adults:</i> IV: 1 mg/dose q5 min (maximum 5 mg) PO: 10–20 mg/dose TID–QID; increase PRN (Usual dose 40–320 mg/24 hr, TID–QID)	Hypotension, syncope, bronchospasm, nausea and vomiting, hypoglycemia, lethargy or depression, heart block	Tab: 10, 20, 40, 60, 80, 90 mg Caps, extended release: 60, 80, 120, 160 mg Oral sol: 20, 40 mg/5 mL Concentrated sol: 80 mg/mL Inj: 1 mg/mL
Prostaglandin E ₁ or alprostadil (Prosta- tin VR, PGE ₁) (Vasodilator)	For patency of ductus arteriosus: IV: Begin infusion at 0.05–0.1 mcg/kg/min When desired effect achieved, reduce to 0.05, 0.025, and 0.01 mcg/kg/min If unresponsive, dose may be increased to 0.4 mcg/kg/min	Apnea, flushing, bradycardia, hypo- tension, fever	Inj: 500 mcg/mL

Protamine sulfate (Heparin antidote)	Antidote to heparin overdose: IV: Each 1 mg protamine neutralizes approx 100 U heparin given in preceding 3-4 hr. Slow IV infusion at rate not exceeding 20 mg/min or 50 mg/10 min. (Check APTT)	Hypotension, bradycardia, dyspnea, flushing, coagulation problem	Inj: 10 mg/mL
Quinidine (Cardioquin, Quinidex, Quinaglute) (Class IA antiarhythmic)	Children: Test dose for idiosyncrasy: 2 mg/kg once (PO as sulfate; IM/IV as gluconate) Therapeutic dose: IV (as gluconate): 2-10 mg/kg/dose, q3-6 hr PRN PO (as sulfate): 15-60 mg/kg/24 hr, q6 hr Adults: Test dose: 200 mg once PO/IM Therapeutic dose: PO (as sulfate, immediate release): 100-600 mg/dose q4-6 hr Begin at 200 mg/dose and titrate to desired effect, or PO (sulfate, sustained release): 300-600 mg/dose q8-12 hr PO (as gluconate): 324-972 mg q8-12 hr IM (as gluconate): 400 mg/dose q4-6 hr IV (as gluconate): 200-400 mg/dose, infused at a rate of ≤ 10 mg/min (<i>Therapeutic level:</i> 3-7 mg/L)	Nausea and vomiting, ventricular arrhythmias, prolonged QRS complex, depressed myocardial contractility, blood dyscrasias, symptoms of cinchonism	<i>Gluconate</i> (62% quinidine): Tab, slow-release: 324 mg Inj: 80 mg/mL <i>Sulfate</i> (83% quinidine): Tabs: 200, 300 mg Tab, slow-release: 300 mg Susp: 10 mg/mL

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Sildenafil (Revatio, Viagra) (Phosphodiesterase type-V inhibitor)	For pulmonary hypertension: <i>Neonates:</i> PO: 0.25-1 mg/kg/dose, BID-QID <i>Infants and Children:</i> PO: 0.25-1 mg/kg/dose, q4-6 hr <i>Adults:</i> PO: 20 mg TID <i>Children:</i> PO: Starting dose 10 mg QD. Increment of 10 mg q6-8 wk to max dose of 40 mg QD as needed (Adult max 80 mg/24 hr) <i>Children:</i> PO: <i>Loading:</i> 3 mg/m ² <i>Maintenance:</i> 1 mg/m ² /day QD <i>Adults:</i> PO: <i>Loading:</i> 6 mg <i>Maintenance:</i> 2 mg/day QD (<i>Therapeutic level:</i> 6-15 ng/mL)	Hypotension, tachycardia, flushing, headache, rash, nausea, diarrhea, priapism, platelet dysfunction, myalgia, paresthesia, blurred vision, epistaxis, dyspnea Contraindicated in concurrent use of organic nitrates Headache, constipation, diarrhea, elevated liver enzymes, rhabdomyolysis, myopathy Hypertension, peripheral edema, chest pain, fever, headache, acne, hirsutism, hypercholesterolemia, neurotoxicity, abdominal pain, anemia, pneumonitis Nausea and vomiting, constipation, severe hypokalemia (muscle weakness, confusion [monitor serum potassium levels, ECG]), hypocalcemia or hypernatremia (edema)	Tab: 20, 25, 50, 100 mg Tab: 5, 10, 20, 40, 80 mg Tab: 1, 2 mg Oral sol: 1 mg/mL Powder: 454, 480 g Susp: 15 g/60 mL
Simvastatin (Zocor) (Antilipemic, HMG-CoA reductase inhibitor) Sirolimus (Rapamune) (Immunosuppressant) Sodium polystyrene sulfonate (Kayexalate, Kionex) (Potassium-removing resin)	For hyperkalemia (slowly effective, taking hours to days): <i>Children:</i> PO, NG: 1 g/kg/dose, q6 hr PR: 1 g/kg/dose, q2-6 hr <i>Adults:</i> PO, NG, PR: 15 g QD-QID (Cation exchange resin with practical exchange rates of 1 mEq potassium per 1 g resin) (NOTE: Delivers 1 mEq sodium for each mEq of potassium removed)		

For SVT and VT:PO: 80–120 mg/m²/24 hr, TID (*infants*) BID (*older children and adults*)

Sotalol
(Betapace)
(Class II and III
antiarrhythmic)

Chest pain, palpitation, hypoglycemia, hypotension, torsades de pointes, nausea and vomiting, abdominal pain, CNS symptoms (depression, weakness, dizziness), bronchospasm, heart block, bradycardia, negative inotropic effects, QT prolongation
(Discontinue if QTc >550 msec)

Tab: 80, 120, 160, 240 mg
Syrup: 5 mg/mL

Spironolactone (Aldactone) (Potassium-sparing diuretic, aldosterone antagonist)	<p><i>Children:</i> PO: 3 mg/kg/24 hr, BID–TID</p> <p><i>Adults:</i> PO: 50–100 mg/24 hr, TID–QID (Max 200 mg/24 hr)</p>	Hyperkalemia (when given with potassium supplements and ACE inhibitors), GI distress, rash, gynecomastia, agranulocytosis Contraindicated in renal failure	Tab: 25, 50, 100 mg Susp: 1, 2, 2.5, 5, 25 mg/mL
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For thrombolysis:

(Use in consultation with a hematologist)

Children:
IV: 3500–4000 U/kg over 30 min, followed by 1000–1500 U/kg/hr, or 2000 U/kg load over 30 min followed by 2000 U/kg/hr
(Duration of infusion based on response but generally does not exceed 3 days. Obtain tests at baseline and q4 hr: APTT, TT, fibrinogen, PT, hematocrit, platelet count. APTT and TT should be <2 times control.)

Potential for allergic reaction with repeated use; premedicate with acetaminophen and antihistamine, and repeat q4–6hr

Inj: 250,000, 750,000,
1,500,000 IU powder for
reconst

Continued

TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Tacrolimus (Prograf) (Immunosuppres- sant)	<i>Children and adults:</i> PO: 0.15–0.4 mg/kg/day, BID IV: 0.03–0.15 mg/kg/day continuous infusion (<i>Therapeutic level:</i> 5–15 ng/mL)	Hypertension, hypotension, peripheral edema, myocardial hypertrophy, chest pain, fever, headache, encephalopathy, pruritus, hypercholesterolemia, electrolyte imbalance, neurotoxicity, nephrotoxicity, diarrhea, anemia, dyspnea	Caps: 0.5, 1, 5 mg Susp: 0.5 mg/mL Inj: 5 mg/mL (1 mL) Inj: 25 mg/mL
Tolazoline (Priscoline) (α -adrenoceptor blocker)	For neonatal pulmonary hypertension: IV: <i>Loading:</i> 1–2 mg/kg over 10 min <i>Maintenance:</i> 1–2 mg/kg/hr	Hypotension and tachycardia, pulmonary hemorrhage, GI bleeding, arrhythmias, thrombocytopenia, leukopenia	
Triamterene (Dyrenium) (Potassium- sparing diuretic)	<i>Children:</i> PO: 2–4 mg/kg/24 hr, QD–BID. May increase up to max 6 mg/kg/24 hr or 300 mg/24 hr <i>Adults:</i> PO: 50–100 mg/24 hr, QD–BID (Max 300 mg/24 hr)	Nausea and vomiting, leg cramps, dizziness, hyperuricemia, rash, prerenal azotemia	Caps: 50, 100 mg

Urokinase (Abbokinase) (Thrombolytic enzyme)	<p>For thrombolysis (in vein thrombosis or pulmonary embolism): (Should be used in consultation with a hematologist)</p> <p><i>Children:</i></p> <p>IV: Loading: 4400 U/kg over 10 min</p> <p>Maintenance: 4400 U/kg/hr for 6–12 hr. Some patients may require 12–72 hr of therapy</p> <p>(Monitor same laboratory tests as for streptokinase)</p> <p>For occluded IV catheter clearance:</p> <p>Aspiration method: Use 5000 U/mL concentrate. Instill into the catheter a volume equal to the internal volume of catheter over 1–2 min, leave in place for 1–4 hr, then aspirate. May repeat with 10,000 U/mL if no response. Do not infuse into the patient</p> <p>IV infusion method: 150–200 U/kg/hr in each lumen for 8–48 hr at a rate of at least 20 mL/hr</p> <p><i>Adults:</i></p> <p>For pulmonary embolism:</p> <p>IV: Priming dose: 4400 U/kg.</p> <p>IV infusion: 4400 U/kg/hr for 12 hr by infusion pump</p>	<p>Bleeding, allergic reactions, rash, fever and chills, bronchospasm</p>	Inj: 5000 U/mL
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TABLE E-1
DOSAGES OF DRUGS USED IN PEDIATRIC CARDIOLOGY (Continued)

DRUG	ROUTE AND DOSAGE	TOXICITY OR SIDE EFFECTS	HOW SUPPLIED
Verapamil (Isoptin, Calan) (Calcium channel blocker, class IV antiarrhythmic)	For dysrhythmia (SVT):		
	<i>Children:</i> IV: 1–15 yr (for SVT): 0.1–0.3 mg/kg over 2 min May repeat same dose in 15 min (Max dose 5 mg first dose; 10 mg second dose)	Hypotension, bradycardia, cardiac depression	Tab: 40, 80, 120 mg Tab, extended release: 120, 180, 240 mg
	<i>Adults:</i> IV: 5–10 mg, 10 mg second dose		Caps, extended release: 100, 120, 180, 200, 240, 300, 360 mg
	For hypertension:		Susp: 50 mg/mL Inj: 2.5 mg/mL
	<i>Children:</i> PO: 4–8 mg/kg/24 hr, TID <i>Adults:</i> PO: 240–480 mg/24 hr, TID		
Vitamin K ₁	Antidote to dicumarol or warfarin:		Tab: 5 mg
	PO/IM/SC/IV: 2.5–10 mg/dose in 1 dose for correction of excessive PT from dicumarol or warfarin overdose		Inj: 2, 10 mg/mL

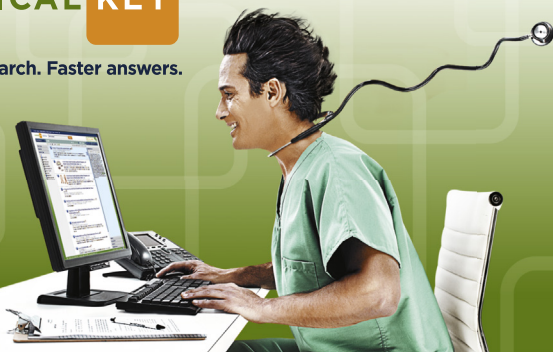
Warfarin (Coumadin, Safarin) (Anticoagulant)	<p>Children: PO: <i>Initial:</i> 0.1–0.2 mg/kg/dose QD in evening for 2 days (Max dose 10 mg/dose) (In liver dysfunction, 0.1 mg/kg/day, max 5 mg/dose) <i>Maintenance:</i> 0.1 mg/kg/24H QD (Monitor INR after 5–7 days of new dosage. Keep INR at 2.5–3.5 for mechanical prosthetic valve; 2–3 for prophylaxis of DVT, pulmonary emboli.) (Heparin preferred initially for rapid anticoagulation; warfarin may be started concomitantly with heparin or may be delayed 3–6 days.)</p> <p>Adults: PO: <i>Initial:</i> 5–15 mg/dose QD for 2–5 days <i>Maintenance:</i> 2–10 mg/day (Adjust dosage based on INR)</p>	<p>Bleeding (antidote: vitamin K or fresh-frozen plasma) <i>Increased PT response:</i> salicylates, acetaminophen, alcohol, lipid-lowering agents, phenytoin, ibuprofen, some antibiotics <i>Decreased PT response:</i> antihistamines, barbiturates, oral contraceptives, vitamin C, diet high in vitamin K Onset of action: 36–72 hr, and full effects in 4–5 days. Mode of action: inhibits hepatic synthesis of vitamin K-dependent factors (I, VII, IX, X)</p>	<p>Tab: 1, 2, 2.5, 3, 4, 5, 6, 7.5, 10 mg Inj: 5 mg</p>
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ACE, angiotensin-converting enzyme; APTT, activated partial thromboplastin time; AV, atrioventricular; BID, two times a day; BP, blood pressure; Caps, capsule; CHF, congestive heart failure; CK, creatine kinase; CNS, central nervous system; CR, controlled release; D₅W, 5% dextrose in water; DVT, deep vein thrombosis; ECG, electrocardiogram; ET, endotracheal; GI, gastrointestinal; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A; HOCM, hypertrophic obstructive cardiomyopathy; IM, intramuscular; Inj, injection; INR, international normalized ratio; IV, intravenous; LFT, liver function test; max, maximum; NE, norepinephrine; NG, nasogastric; NS, normal saline; PDA, patent ductus arteriosus; PG, prostaglandin; PO, by mouth; PR, per rectum; PRN, as necessary; PT, prothrombin time; q, every; QD, once a day; QID, 4 times a day; QOD, every other day; RBF, renal blood flow; reconst, reconstitution; SC, subcutaneous; sol, solution; Supp, suppository; Susp, suspension; Tab, tablet; TDD, total digitalizing dose; TID, three times a day; TI, thrombin time; WBC, white blood cell; (±), may occur.

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